

## **The effects of TJ-14 (Hange-shashin-to), Japanese kampo medicines, on spontaneous electrical activity of circular smooth muscle cells in the mouse proximal colon**

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The Japanese kampo medicine TJ-14 have been used to treat diarrhea. Previously, it was shown that TJ-14 inhibits spontaneous contractions of circular smooth muscle cells (CSMCs) in the rat distal colon (Am J Physiol, 2012). However, it is still unclear how these drugs precisely act on spontaneous electrical activity in the colon. Therefore, electrophysiological effects of TJ-14 on CSMCs of the mouse proximal colon were investigated by using intracellular membrane potential recording techniques. TJ-14 evoked triple responses: transient hyperpolarization, slow depolarization and slow hyperpolarization. Transient hyperpolarization was partially inhibited by L-NNA, an inhibitor of nitric oxide synthase. The residual hyperpolarization was abolished by bupivacaine, a blocker of pH-sensitive K<sup>+</sup> channel. Slow hyperpolarization was associated with the reduction of membrane noises. NPPB, a Ca<sup>2+</sup> - activated Cl<sup>-</sup> channel (CaCC) inhibitor, or bumetanide, a Na<sup>+</sup> - K<sup>+</sup> - 2Cl<sup>-</sup> co-transporter (NKCC1) inhibitor, also hyperpolarized the membrane and inhibited the membrane noises. Since CaCCs and NKCC1 are expressed only in interstitial cells of Cajal (ICC) in the mouse colon, the membrane noises seem to originate in ICC. These results suggest that TJ-14 inhibits contractile activities of the mouse proximal colon by affecting both CSMCs and ICC.