
**ABSTRACT**
Flavonoids, compounds containing a 2- phenylbenzo(γ)pyrane nucleus, are universally distributed among vascular plants. Even though flavonoids are ingested in a normal diet in average quantities of 1 g daily, their effects on the digestive system have only been recently investigated. This study used an in vitro model of colonic secretion, monolayers of Tg4 colonic adenocarcinoma cells mounted in Ussing chambers, to demonstrate that 100 µmol/L of either tangeritin or nobiletin, polymethoxylated flavonoids contained in citrus fruits, stimulated sustained electrogenic chloride secretion with a maximal short-circuit current of 3.3 μA/cm². In contrast, naringin and hesperidin, glycosylated citrus flavonoids, stimulated minimal secretion, suggesting that carbohydrate substitutions inhibited their secretory potential. The secretion stimulated by tangeritin and nobiletin was synergistic with carbachol but not with vasoactive intestinal peptide and was inhibited by barium chloride, bumetanide, H-89, and Cl⁻ depletion. These properties suggest that tangeritin and nobiletin stimulated Cl⁻ secretion via the cAMP pathway; however, these flavonoids did not stimulate cAMP production to the extent seen with vasoactive intestinal peptide. These flavonoids did not autooxidize, suggesting that reactive oxygen species did not mediate this secretion. These observations suggest that dietary citrus flavonoids may modulate colonic secretion, possibly through direct interaction with intracellular secretory pathways.