(2R,3S,2'' R,3''R)-manniflavanone, a new gastrointestinal smooth muscle L-type calcium channel inhibitor, which underlies the spasmolytic properties of Garcinia buchananii stem bark extract

Abstract:
Garcinia buchananii Baker stem bark extract (GBB) is a traditional medication of diarrhea and dysentery in sub-Saharan Africa. It is believed that GBB causes gastrointestinal smooth muscle relaxation. The aim of this study was to determine whether GBB has spasmolytic actions and identify compounds underlying these actions. Calcium (Ca(2+)) imaging was used to analyze the effect of GBB on Ca(2+) flashes and Ca(2+) waves in guinea pig gallbladder and distal colon smooth muscle. Intracellular microelectrode recording was used to determine the effect of GBB, six fractions of GBB, M1-5 and M7, and (2R,3S,2'' R,3''R)-manniflavanone, a compound isolated from M3 on action potentials in gallbladder smooth muscle. The technique was also used to analyze the effect of GBB, M3, and (2R,3S,2'' R,3''R)-manniflavanone on action potentials in the circular muscle of mouse and guinea pig distal colons, and the effect of GBB and (2R,3S,2''R,3'' R)-manniflavanone on slow waves in porcine ileum. GBB inhibited Ca(2+) flashes and Ca(2+) waves. GBB, M3 and (2R,3 S,2''R,3''R)-manniflavanone inhibited action potentials. L-type Ca(2+) channel activator Bay K 8644 increased the discharge of action potentials in mouse colon but did not
trigger or increase action potentials in the presence of GBB and (2R,3S,2"R,3"R)-manniflavanone. GBB and (2R,3S,2"R,3"R)-manniflavanone inhibited action potentials in the presence of Bay K 8644. GBB and (2R,3S,2"R,3"R)-manniflavanone reduced the amplitude but did not alter the frequency of slow waves in the porcine ileum. In conclusion, GBB and (2R,3S,2"R,3"R)-manniflavanone relax smooth muscle by inhibiting L-type Ca(2+) channels, thus have potential for use as therapies of gastrointestinal smooth muscle spasms, and arrhythmias.

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