Quinine blocks 5-HT and 5-HT_3 receptor mediated peristalsis in both guinea pig and mouse ileum tissue

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Introduction. Quinine is commonly used to treat malaria; however one of the principal side effects is gastrointestinal disturbances (White, 1992). 5-HT_3 receptors modulate gut peristalsis (Chetty *et al.,* 2006), and, as quinine has been shown to act as a 5-HT_3 receptor antagonist (Thompson and Lummis, 2008) it is possible that these side effects result from actions at gut 5-HT_3 receptors. To address this question, we examined the ability of quinine to antagonise 5-HT and 5-HT_3 mediated peristalsis in guinea pig and mouse ileum.

Methods. Ileum was excised from male guinea pigs (200-300g) and C57BL/6 mice (25-35g) following cervical dislocation. Ileum segments (3-5 cm) were mounted in 50 ml organ baths containing Tryode's solution at 35-37 ℃. Concentration-response curves were constructed for 5-HT and the selective 5-HT_3 agonist 2-Me-5-HT (non-cumulative doses). Quinine was pre-applied for 10 min and inhibition measured using agonist concentrations that elicited a submaximal response.

Results. Concentration-dependent contractions produced by 5-HT (pEC_{50} = 5.45 ± 0.17, n =8) and the selective 5-HT_3 agonist 2-Me-5-HT (5.01 ± 0.17, n = 11) were not significantly different (Student's t-test, t = 0.619, df = 17, p = 0.544) in guinea pig ileum. Increasing concentrations of quinine were able to antagonise the activities of both 5-HT (pIC_{50} = 5.03 ± 0.2, n = 6) and 2-Me-5HT (pIC_{50} = 4.59 ± 0.26, n = 4). At mouse ileum, 5-HT (pEC_{50}= 7.57 ± 0.33, n = 9) was more potent (Student's t-test, t = 3.6, df = 12, p = 0.004) than 2-Me-5-HT (pEC_{50} = 5.45 ± 0.58, n = 5). Quinine antagonised both the 5-HT (pIC_{50} = 4.87 ± 0.31, n = 7) and 2-Me-5-HT-induced (pIC_{50} = 6.18 ± 1.14, n = 4) contractions.

Conclusions. These results support previous electrophysiological studies that identified quinine as an antagonist at recombinant 5-HT_3 receptors with IC_{50} values comparable with those reported here (pIC_{50} = 4.87, Thompson *et al*., 2007). Further, we found that quinine completely blocked 5-HT induced contractions in mouse and guinea pig, raising the possibility that quinine targets other 5-HT receptors in the gut (e.g., 5-HT_4 receptors) and may influence intestinal function.

Chetty *et al*., (2006). *Br.J.Pharmacol*., 148; 112-141.
Thompson *et al*., (2007). *Br.J.Pharmacol* 151; 666-667.
Thompson and Lummis, (2008). *Br.J.Pharmacol* 153; 1686-96. White, (1992). *BJCP*, 34; 1-10.