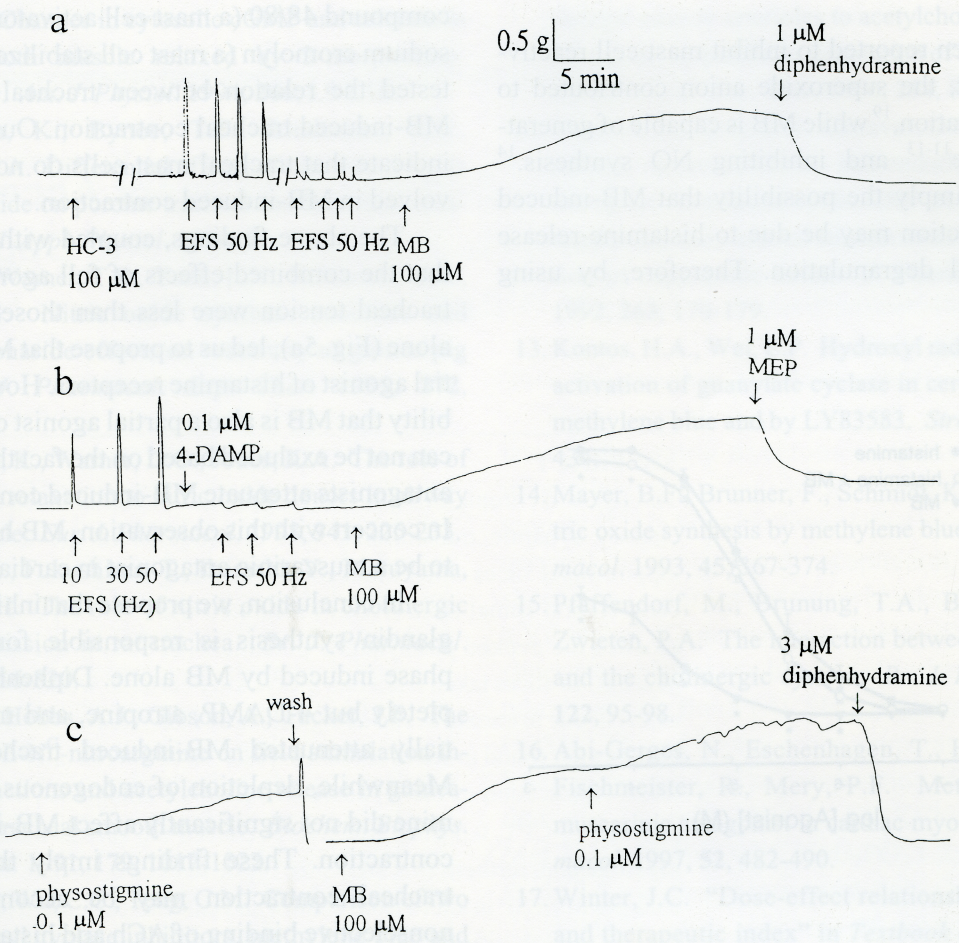

Fig. 4. Representative curves illustrating the effects of hemicholinium-3 (HC-3) (a), 4-DAMP (b), and physostigmine (c) on electrical field stimulation (EFS)-induced cholinergic tracheal contraction and/or methylene blue (MB)-induced contraction. (a) HC-3 (100 μM) was added 30 min before EFS. The MB-induced contractions were significantly inhibited 45 min after HC-3 was added. Traces are representative of at least 5 separate experiments. Indomethacin (3 μM) was present throughout.

ceptor also plays a role in MB-induced tracheal contraction. These results led us to speculate that MB could modulate not only muscarinic but also histamine receptors in guinea pig tracheal smooth muscle. Such modulation may involve various mechanisms, including augmentation of ACh release from cholinergic fibers, inhibition of cholinesterase, augmentation of histamine release from mast cells, or direct binding to muscarinic and histamine receptors.

To elucidate the relation between MB-induced tracheal contraction and the cholinergic system, we used the ACh synthesis inhibitor hemicholinium-3 (100 μM) and the sodium channel blocker, tetrodotoxin (0.3 μM). Our results (Figs. 3, 4a) indicate that endogenous ACh is less likely to be involved in MB-induced tracheal contraction. Similarly, endogenous histamine depletion did not significantly affect MB-induced tracheal contraction (Fig. 3). On the other hand, we observed that the cholinerase inhibitor, physostigmine (0.1 μM), increased both inherent tracheal muscular tension and MB-induced tracheal contraction (Fig. 4c). This result indicates that endogenous ACh regulates the inherent muscular tension in guinea pig trachea, and that MB seems unlikely to be a cholinerase inhibi-