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Mechanism Involved in Methylene Blue-induced Tension Changes in Isolated Guinea Pig Trachea

Duen-Suey Chou, MS, Doctoral Student
George Hsiao, PhD
Tzeng-Fu Chen, PhD
Joen-Rong Sheu, PhD
Department of Pharmacology, Taipei Medical University

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ABSTRACT

In this study, we explore the possible mechanism of methylene blue (MB)-induced tension changes in isolated guinea pig trachea. MB alone decreased inherent tracheal tension, whereas, indomethacin caused a depression of MB-induced relaxation leading to the appearance of concentration-dependent contraction. On the other hand, diphenhydramine completely but 4-diphenylacetoxy-N-methylpiperidine methiodine (4-DAMP), atropine, and mepyramine each partially attenuated MB-induced tracheal contraction. The maximum inhibitions by atropine, 4-DAMP, and mepyramine were 88.4% ± 3.9% (n = 6), 80.3% ± 4.3% (n = 6), and 72.3% ± 3.3% (n = 6), respectively. This reveals that MB not only modulates muscarinic but also histamine receptors in guinea pig tracheal smooth muscle. Moreover, depletion of endogenous acetylcholine (ACh) and histamine by using hemicholinium-3 and compound 48/80 did not significantly affect MB-induced tracheal contraction. The combined effect of histamine and MB on the increase of tracheal tension being less than that of histamine alone at higher concentrations suggests that MB is a partial agonist of histamine receptors. The possibility that MB is also a partial agonist of ACh receptors can not be excluded based on the fact that ACh receptor antagonists attenuate MB-induced contraction. In conclusion, we propose that the inhibition of prostaglandin synthesis is responsible for the relaxation phase induced by MB, and that the nonselective binding of ACh and histamine receptors contributes to MB-induced tracheal contraction. (N. Taipei J. Med. 2001; 3:18-25)

INTRODUCTION

Methyl blue (MB) is generally assumed to be an inhibitor of nitric oxide (NO)-activated soluble guanylate cyclase (sGC) in various tissues.[1] NO plays an important physiologic role in several biological systems, including airway smooth muscle.[2-6] In analysis of the NO pathway, MB is often used as a pharmacological tool. There is evidence that MB and the NO inhibitor, N^G-monomethyl-L-arginine (L-NMA), enhance chol-

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Correspondence: Duen-Suey Chou
Department of Pharmacology, Taipei Medical University,
250 Wu Hsing Street, Taipei 110-31, Taiwan, R.O.C.
Tel: 886-2-27361661 ext. 580; Fax: 886-2-27361661 ext. 580
E-mail: fird@mail.tmc.edu.tw