SUMMARY AND CONCLUSION

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In the present work, the effect of verapamil on the smooth muscles of trachea and blood vessels was investigated.

In vitro: the effect of verapamil, a calcium antagonist, was studied on histamine and acetylcholine contractions of isolated guinea-pig tracheal strips as well as perfused lung preparations. Also, the effect of verapamil on K^+ -induced contractions of isolated rabbit aortic strip preparations and its effect on the perfusate of the isolated perfused rat hind quarters was evaluated. Moreover, *in vivo* experiments were done to demonstrate the effect of verapamil against bronchoconstriction induced by histamine or acetylcholine inhalation in normal guinea-pigs and antigen inhalation in sensitized animals.

The data revealed that, verapamil was found to inhibit histamine and acetylcholine-induced contractions of the isolated guinea-pig tracheal strip. Furthermore, it inhibited the preparation when added on top of the already present contraction. The effect of verapamil was dose dependent as the inhibition was increased by increasing the dose of the drug. The mechanical response of the guinea-pig tracheal muscle to histamine was much

reduced after the addition of verapamil than its response to acetylcholine. This might be explained on the ground that histamine-induced contractions are more dependent on extracellular ionic calcium than those induced by acetylcholine.

Verapamil, also, inhibited the spasmogenic effect of KCl on the isolated rabbit aortic strips.

These *in vitro* results suggested that verapamil might act as a bronchodilator in the guinea-pig *in vivo*. To test this hypothesis, protection produced by verapamil against histamine, acetylcholine and antigen-induced bronchospasm in normal and sensitized guinea-pigs was investigated. Verapamil significantly prolonged the preconvulsive time of unsensitized guinea-pigs exposed to histamine or acetylcholine aerosol . Verapamil, also, prolonged the preconvulsive time of sensitized guinea-pigs exposed to the inhalation of the antigen aerosol. The protection acquired by verapamil in the sensitized animals exposed to the inhalation of the antigen is more than the protection induced by verapamil in the normal guinea-pigs exposed to inhalation of histamine or acetylcholine. The data may suggest that the beneficial effect of calcium antagonists in allergic bronchoconstriction may be predominantly on the mast cell degranulation.

In conclusion, the present results suggest that verapamil may serve as bronchodilator, stabilizer of the airways and can prevent bronchoconstriction.