ABSTRACT

Isolation of a Muscarinic Alkaloid with Ocular Hypotensive Effect from *Trophis racemosa*

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In this study, an alkaloid (T.S) was extracted from *Trophis racemosa*, a plant used in Jamaican folklore to improve vision. The extraction and purification procedures involved various chromatographic techniques, which were used in conjunction with infrared and ultra violet spectral analyses to identify quaternary nitrogen in the molecular structure of the alkaloid.

In pharmacological studies, the alkaloid was used as the chloride salt. Aqueous solutions (0.5%, 1% and 2%) of this chloride salt of the alkaloid reduced intra-ocular pressure (IOP), ranging from a fall of 6.6 ± 0.7 mmHg to 15.7 ± 0.3 mmHg, in a dose dependent manner when applied topically to the dog's eye. Pretreatment of the dog's eye with the muscarinic antagonist, atropine (1%), inhibited the alkaloid-induced reduction of intra-ocular pressure. Similar inhibition of the alkaloid-induced fall in IOP was also obtained after pretreatment of the dog's eye with a dose of pirenzepine (0.1mL of a 0.5% solution) that blocks both M_1 and M_3 receptors. There was also no inhibition of the alkaloid-induced fall in IOP by the alpha adrenoceptor antagonist, phenoxybenzamine (0.1 mL of a 1% solution). But in the presence of isoprenaline (0.1mL of a 1% solution), a beta adrenoceptor agonist which relaxes the ciliary muscle, there was inhibition of

the fall in intra-ocular pressure produced by the alkaloid, T.S, and also by pilocarpine (0.5%), a muscarinic agonist.

On isolated sections of guinea-pig ileum and guinea-pig trachea, the alkaloid (T.S) at 50μg/mL produced contractions which were inhibited by atropine (0.4μg/mL) and by pirenzepine at a dose of 1.3 μg/mL which blocks muscarinic M_1 and M_3 receptors. However, when pirenzepine was given at a dose (3ng/mL) which selectively blocked contractions produced by the M_1 agonist, McN-A343, it did not inhibit contractions produced by the alkaloid. There was also no inhibition of the alkaloid-induced contractions of the guinea-pig ileum in the presence of blockade of ganglionic nicotinic receptors with hexamethonium (0.6 μg/mL) and pentolinium (0.3μg/mL), although nicotine-induced (10μg/mL) contractions were inhibited in the presence of these nicotinic ganglion blockers.

On the rat's blood pressure, the alkaloid and pilocarpine produced an initial fall followed by a rise. The fall was blocked by a dose of pirenzepine (0.24μg/Kg) that inhibited M_1 and M_3 receptors. However, the pressor phase of the blood pressure response of both pilocarpine and the alkaloid (T.S) was equally blocked in the presence of the nicotinic ganglionic blocker, pentolinium and also in the presence of phentolamine, an alpha adrenoceptor antagonist.

From these results, it is concluded that an alkaloid (T.S) with a quaternary nitrogen in its structure, was extracted from *Trophis racemosa*. This alkaloid has

ocular hypotensive effect, which appeared to have been mediated via muscarinic M_3 receptors on the ciliary muscle. The alkaloid also has a minor nicotinic action, but the muscarinic agonist effects masked this nicotinic effect.