

**A few further experiments with pituria / by Sydney Ringer and William Murrell.**

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229

8



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**A FEW FURTHER EXPERIMENTS WITH PITURIA.**

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IN a previous communication in this *Journal* (Vol. I. No. 5) we showed that pituria, the alkaloid of pituri, a solanaceous plant, and belonging to the subdivision Duboisia, manifests many of the properties of atropia. Pituria causes drowsiness, dilates the pupil, produces general weakness with convulsive twitchings, and antagonizes the action of muscarin on the heart. It possesses, however, two properties distinct from those of atropia; it produces sickness and increases the salivary secretion in large doses copiously. Even in the properties in which pituri resembles atropia there are still points of difference. For atropia chiefly dries the mouth and dilates the pupil, and these effects endure many hours, indeed the dilatation of the pupil may last even days, whilst only large doses produce drowsiness, general weakness and twitchings, or quicken the respirations. On the other hand, the earliest effect of pituria is manifested on the breathing, which becomes quick and shallow; then follow general weakness, and, after large doses, severe muscular twitchings, whilst the pupil undergoes far less dilatation, and that lasting a shorter time than after atropia.

Further investigations on the human subject<sup>1</sup> have for the most part confirmed these observations and increased our knowledge of the drug. We find that  $\frac{1}{10}$  to  $\frac{1}{8}$  gr. of nitrate of pituria given hypodermically produces general weakness, slight rhythmic tremor, quickens the pulse and respirations, and produces general perspiration, in some cases slightly, in others abundant. All these symptoms last a short time only, disappearing in half an hour, or even in a shorter time. This dose never dried the mouth nor produced salivation. Moreover, instead of dilating the pupils it always produced slight contraction; therefore we conclude, that when given internally small doses contract but large doses dilate the pupil; and probably, though we have no observations to prove this, large doses first contract and then dilate the pupil.

<sup>1</sup> *Lancet*, March 1, 1879.

In our previous communication we showed that pituri antagonizes the action of muscarin on the heart. We now record some experiments showing that it antagonizes the action of pilocarpine on the heart<sup>1</sup>.

The following experiments were made in January on the exposed hearts of brainless frogs. We used a solution of nitrate of pituria, and in the first experiments a 2 p. c. solution of nitrate of pilocarpine, and afterwards a 10 p. c. solution.

Exp. 1. To a heart, beating at 52 per minute, we applied a small quantity of a 2 p. c. solution of nitrate of pilocarpine, and in half a minute the heart stopped. Soon after we applied a small quantity of a 1 p. c. solution of nitrate of pituria, and in 15 seconds the heart began to beat again, and in one minute beat strongly at 24 per minute: in three minutes at 32, and soon after at 40. In 34 minutes the beats became very feeble at 32 per minute, and we again applied a little of the pituria solution, when the beats rose to 40 and became much stronger, so remaining during the next quarter of an hour, when we suspended our experiments. Seven hours afterwards the heart beat fairly well at 22 per minute.

In the three following experiments the effect of the pilocarpine was rather different. As sometimes happens with muscarin, the pilocarpine did not greatly slow, but greatly weakened the heart's contractions, and the pituria increased both their frequency and especially their strength.

Exp. 2. With the heart's contractions at 44 per minute, we applied some of the pilocarpine solution. In seven minutes the beats fell to 20; in the next twenty minutes they rose to 28; but the contractions became extremely feeble. We then applied the pituria solution, and in one minute the beats became stronger and rose to 40, and in two minutes to 44 good beats per minute. In ten minutes, whilst still beating 44, the contractions became very feeble, but on again applying some pituria the contractions at once grew stronger, though in six minutes they again grew feeble.

Exp. 3. Whilst the heart beat well at 48 we applied the pilocarpine solution, and in nine minutes the pulsations fell to 28 and became feeble; in twenty-five minutes, whilst at 32, they became very feeble. Then on applying pituria the beats in half a minute grew much stronger, rising in six minutes to 40. In nine minutes the heart beat strongly at 48 per minute, and seven hours afterwards it beat fairly well at 28.

Exp. 4. To a heart beating at 52 we applied pilocarpine and the pulsations at once fell to 24, but in the course of fifteen minutes they rose to 36 and became very feeble. We then applied nitrate of pituria, and at once the contractions became much stronger, the cavities contracting fairly well at 34. In eight minutes the beats rose to 40. Four hours after the application of the pituria the heart beat fairly well at 20.

<sup>1</sup> The pituri we used was given us by Mr MacAlister, through Mr E. A. Clare, of the Queensland section of the Paris Exhibition. It was grown in the Botanic Gardens at Brisbane by Mr Hill. Mr Gerrard extracted the alkaloid and prepared the nitrate for us.

Exp. 5. We applied a little of a 10 p. c. solution of nitrate of pilocarpine to a heart beating at 40 per minute. The heart stopped almost immediately in wide diastole. After two minutes of complete arrest a little pituria was applied about every half minute. During the next eight minutes the heart gave a strong contraction, and after eight minutes it suddenly commenced beating strongly at 30 per minute, and so continued during the time we watched it, that is the next ten minutes.

*Antagonism between pituria and pilocarpine on the frog's heart.*

Date.	Decrease after application of pilocarpine.	Loss of strength after application of pilocarpine.	Increased frequency after application of pituria.	Increased strength after application of pituria.	Contractions continued more than
Jan. 1	Heart stopped	Heart stopped	40 beats	became strong	seven hours
" 1	16 beats	extremely feeble	12 beats	"	
" 1	16 beats	"	12 beats	"	seven hours
" 2	16 beats	"	4 beats	"	four hours
" 2	Heart stopped	Heart stopped	30 beats	"	

We see then that pituria will quicken and greatly strengthen a heart slowed and much weakened by pilocarpine, and even restore the contractions to a heart arrested by pilocarpine. In respect therefore to its antagonism to muscarin and pilocarpine, the solanaceous plant pituri acts like the alkaloids from other solanaceous plants, for instance atropia and duboisia.

As pituria, like atropia, antagonizes the action of muscarin and pilocarpine on the frog's heart, we were anxious to know if pituria, like atropia, paralyses the inhibitory apparatus of the heart. Mr Waters, of the Physiological Laboratory at Cambridge, kindly performed this experiment for us, and finds that pituria has by itself no direct effect on the number or force of the heart's contractions, but so affects the vagi that electric stimulation of them no longer slows or arrests the heart but increases the frequency of the beats.

Pituri therefore is more closely allied to tobacco, as Baron Müller has suggested, than to any other solanaceous plant, for tobacco contracts the pupil, topically applied to the eye or when administered by the stomach. It also causes salivation and perspiration, great weakness, and sometimes violent muscular tremblings.