(iii) Our figures for 5-HT are calculated as base. Dr. Bruce mentions "serotonin" (Bruce, 1960) and "indole derivatives" (Bruce, 1961). If his results are calculated using 5-HT creatinine sulphate as his standard then his published results would need to be halved. This would bring them more in line with the above results.

The likelihood of an erroneous diagnosis of a carcinoid tumour by pineapple ingestion is, in our opinion, small. It would surely be much more likely to occur in countries where the staple diet contains 5-HT, as in parts of West Africa where plantains (containing large amounts of this substance) are ingested regularly (Foy and Parratt, 1960).

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REFERENCES

Amin, A. H., Crawford, T. B. B. and Gaddum, J. H. (1954). *J. Physiol.*, **126**, 596–618.
Bruce, D. W. (1960). *Nature, Lond.*, **188**, 147.
Bruce, D. W. (1961). *J. Pharm. Pharmacol.*, **13**, 256.
Collier, H. O. J. and Chesher, G. B. (1956). *Brit. J. Pharmacol.*, **11**, 186–189.
Erspamer, V. (1940). *Arch. exp. Path. Pharmak.*, **196**, 366–390.
Foy, J. M. and Parratt, J. R. (1960). *J. Pharm. Pharmacol.*, **12**, 360–364.
Parratt, J. R. (1958). *Ph.D. Thesis*, University of London, pp. 43–46.
West, G. B. (1960). *J. Pharm. Pharmacol.*, **12**, 768.

The Effects of Gallamine, Carbachol, Nicotine, Ryanodine and Protoveratrine A and B upon Flux of Calcium-47 in Frog Skeletal Muscle

SIR,—We recently reported the effects of tubocurarine, decamethonium, suxamethonium, edrophonium and neostigmine on $^{47}Ca^{++}$-uptake and release in frog sartorius muscle, and compared these with their influence upon uptake and release of $^{42}K^{+}$ and on $^{24}Na^{+}$-uptake (Ahmad and Lewis, 1961). Using similar techniques, we have extended our observations to make a preliminary study of the effects of gallamine, carbachol, nicotine, ryanodine and protoveratrine A and B.

From 1 to 8 mg./ml. of gallamine did not significantly alter $^{47}Ca^{++}$-uptake ($P = 0{\cdot}4 < 0{\cdot}3$) or release. At similar dose levels there was no significant change in $^{42}K^{+}$-uptake ($P = 0{\cdot}2 < 0{\cdot}1$) or release, or in $^{24}Na^{+}$-uptake ($P = 0{\cdot}7 < 0{\cdot}6$).

Carbachol (5 mg./ml.), did not significantly alter uptake of $^{47}Ca^{++}$ ($P = 0{\cdot}3 < 0{\cdot}2$) but its effects upon release were variable. It caused depression of $^{42}K^{+}$-uptake ($P = 0{\cdot}1 < 0{\cdot}05$) with a slight increase in its release but there was no change in $^{24}Na^{+}$-uptake ($P = 0{\cdot}8 < 0{\cdot}7$).

The effects of nicotine were more striking than those of gallamine or carbachol. 1 mg./ml. of nicotine caused a very significant increase in $^{47}Ca^{++}$-uptake ($P = > 0{\cdot}001$), $^{47}Ca^{++}$-release and $^{42}K^{+}$-release. It also markedly decreased $^{42}K^{+}$-uptake ($P = > 0{\cdot}001$) and significantly increased $^{24}Na^{+}$-uptake ($P = > 0{\cdot}02$).

Ryanodine at bath concentrations of 10 to 100 μg./ml. increased markedly both release, and uptake ($P = 0{\cdot}01 < 0{\cdot}001$) of $^{47}Ca^{++}$. With 50 μg./ml. of

ryanodine, $^{42}K^+$-uptake was markedly depressed ($P = >0{\cdot}001$), there was a marked release of $^{42}K^+$, and an increase in $^{24}Na^+$-uptake ($P = >0{\cdot}001$).

Protoveratrine A and B had qualitatively similar effects, but protoveratrine A appeared to be more potent. At doses of 100 μg. to 0·5 mg./ml. both depressed $^{47}Ca^{++}$-uptake (protoveratrine A, $P = 0{\cdot}05 < 0{\cdot}02$; protoveratrine B, $P = 0{\cdot}05 < 0{\cdot}02$) and caused an increased release of $^{47}Ca^{++}$. This confirms the findings of Lister and Lewis (1959) using protoveratrine A. $^{42}K^+$-uptake was not significantly (protoveratrine A, $P = 0{\cdot}4 < 0{\cdot}3$; protoveratrine B, $P = 0{\cdot}2 < 0{\cdot}1$) but $^{24}Na^+$-uptake was markedly increased (protoveratrine A, $P = > 0{\cdot}001$; protoveratrine B, $P = 0{\cdot}2 < 0{\cdot}1$). In some experiments a slightly increased release of $^{42}K^+$ occurred.

These preliminary findings show that compounds capable of causing contracture of the isolated frog sartorius muscle increased both the release of calcium and potassium, and at the same time increased the uptake of calcium and sodium but depressed that of potassium. The more striking effects of ryanodine and nicotine are probably associated with their ability to cause a marked contractural response in skeletal muscle. The lesser effects of carbachol can perhaps be attributed to its low contracture-producing potency at the dose levels used, while protoveratrine does not cause its characteristic response in non-stimulated muscle.

Our results with ryanodine and nicotine are not unlike those of Bianchi and Shanes (1959) and Shanes and Bianchi (1960) who demonstrated that potassium depolarisation and electrical stimulation of the frog sartorius muscle were associated with an increase in both inward and outward fluxes of calcium. When ryanodine and nicotine are used, calcium may become more mobile and is perhaps displaced from combination with a carrier or receptor. This may result in the breakdown of barriers which retain potassium within the cell and sodium outside.

Shanes and his colleagues (1959) from experiments on the voltage-clamped squid axon, suggested that at lower levels of depolarisation, multivalent ions may react with sites on the cell membrane to reduce the number of these available for the passage through of monovalent ions. At higher levels of depolarisation more sites become available due to the displacement of the calcium ions. Our findings appear to be compatible with this view.

We hope to report our results more fully at a later date.

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REFERENCES

Ahmad, K. and Lewis, J. J. (1961). *J. Pharm. Pharmacol.*, **13**, 123–127.
Bianchi, C. P. and Shanes, A. M. (1959). *J. gen. Physiol.*, **42**, 803–815.
Lister, R. E. and Lewis, J. J. (1959). *J. Pharm. Pharmacol.*, **11**, *Suppl.*, 176*T*–184*T*.
Shanes, A. M. and Bianchi, C. P. (1960). *J. gen. Physiol.*, **43**, 481–493.
Shanes, A. M., Freygang, W. H., Grundfest, H. and Amatniek, E. (1959). *Ibid.*, **42**, 793–802.