Actions of a multi-component medication, SKT, on skeletal, smooth and cardiac muscle

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INTRODUCTION

To investigate the actions of Shakuyaku-kanzo-to (SKT), a standardized 1:1 combination of two root powder extracts, paeony and licorice, we have studied its actions and those of its components on skeletal, smooth and cardiac muscle.

METHODS

The skeletal muscle experiments were performed on guinea-pig and rat phrenic nerve-diaphragm preparation using phrenic nerve stimulation and direct muscle stimulation. Smooth muscle experiments were done on guinea-pig ileum using the Magnus method to record both resting tension and responses to field stimulation. Whole heart experiments were performed on guinea-pig using Langendorff perfusion. The guinea-pigs were Duncan Hartley, 300-500g. Rats were male Long Evans or Wistar, 200-500g. Both were stunned by cervical dislocation.

RESULTS

We found (1) A large difference in time course of inhibition of contraction in smooth and skeletal muscles. In skeletal muscles the full effect develops over 20-30 minutes. By contrast in smooth muscle both resting and stimulated tension fall completely within 1-2 minutes. (2) The action on skeletal muscle is directly on the muscle, not necessarily or primarily on neuromuscular transmission. (3) The dose-response curve in skeletal muscle was found to be very steep, with a threshold around 1 mg/ml, and full inhibition around10 mg/ml. (4) Conditions for actions at lower concentrations are shown in a second poster. (5) Experiments at 0.2mg/ml on Langendorff perfused whole heart show a small increase in force before a small slow fall.

FIGURE LEGENDS

Figure 1. Relaxing effect of SKT 10mg/ml on ileum muscle preparation in response to repeated nerve stimulation. The vertical line shows the time at which TJ-68 was added. Both resting and active tension are reduced within 1-2 minutes.

Figure 2. Relaxing effect of SKT 10mg/ml on diaphragm muscle preparation in response to repeated nerve stimulation. The vertical line shows the time at which TJ-68 was added. The twitch tension is reduced within 30 minutes.

Figure 3. Experiment to show that SKT 10 mg/ml acts directly on skeletal muscle, not solely through nervous innervation. Responses both to nerve and direct muscle stimulation are abolished.

Figure 4. Dose-response curve in skeletal muscle. Threshold dose is around 1 mg/ml. IC50 is about 5 mg/ml. Almost total abolition at 10 mg/ml. The does-response curve is much steeper than for a single drug-receptor interaction.

CONCLUSION

These results could be consistent with synergistic actions between multiple components but also with the idea that there is a cascade of events in a regulatory network of interactions. The time course of action in skeletal muscle sometimes appears to be step-wise, which might indicate that the cascades develop with different time course in different motor units. Further experimental work is required to investigate these and other possibilities.

Acknowledgements

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Reference: Sam, Terrar, Noble, Tasaki & Noble (2015) Extracellular potassium may potentiate the action of a multi-component medication, SKT, in skeletal muscle. Poster, Cardiff Meeting.

Figure 1

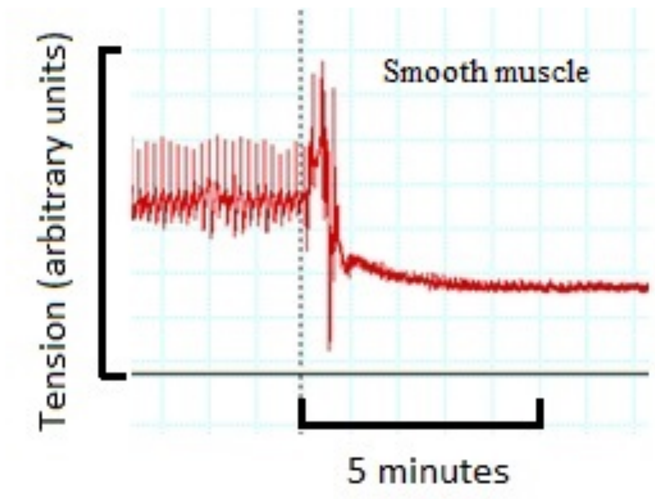

Figure 2

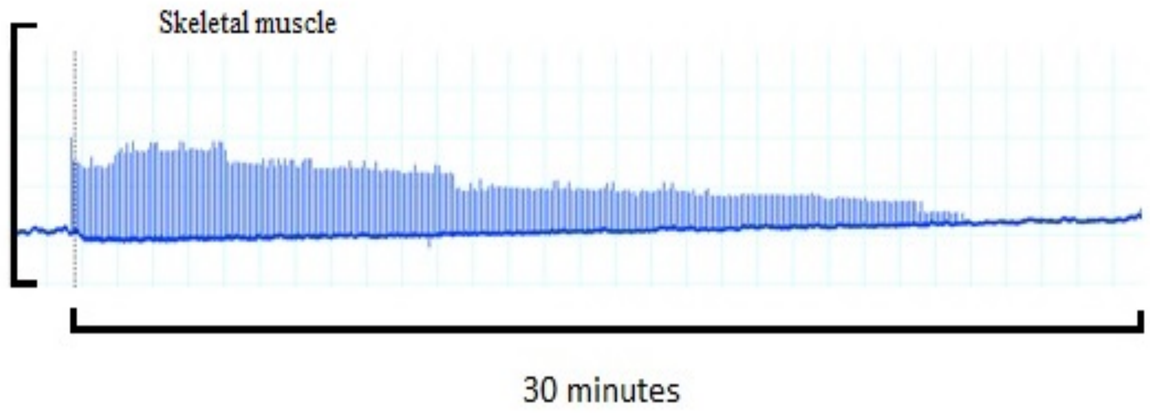

Figure 3

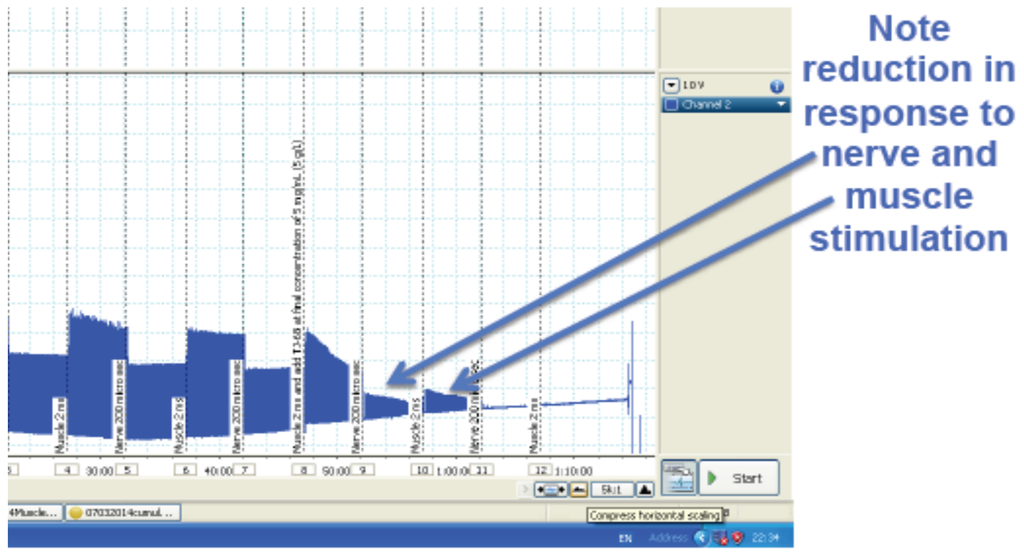

Figure 4