THE PHARMACOLOGICAL ACTIONS OF GINSENG ON CARDIOVASCULAR SYSTEM

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It was found that Panax Ginsen extract has a hypotensive action when injected into dogs. The present study is involved with the mechanism of the hypotensive action of Panax Ginsen. To investigate this mechanism, it is proper to consider the current concept on the excitation contraction coupling processes of muscle in general and that of smooth muscle in particular.

Upon the arrival of a propagated excitation wave, the muscle cell undergoes rapid depolarization and transient reversal of polarity, followed by a gradual restoration of the resting membrane potential. This sequence of changes is designated as the transmembrane action potential. Recognition of the existence of transversely and longitudinally oriented membranelimited channels in the sarcoplasm suggested the possible participation of these structures in the internally transmitted signal from the surface membrane to the contractile element, actomyosin, throughout the muscle cell. For example, electrical stimulation of skinned fibers caused contraction, which indicates that intracellular membranes may conduct electrical signals. A concept of intracellular transmission of excitation by means of a sarcoplasmic reticulum is an attractive hypothesis, but supporting evidence is circumstantial. The internally propagated conduction of the membrane excitation signal appears to be applicable, especially in skeletal muscle, where the time lapse between membrane excitation and contractile response is short and the size of muscle fiber is large. However, in view of the slow time course of contraction, the smaller size of heart and smooth muscle fibers and the paucity of the reticulum system in the heart and smooth muscle make internal spread of membrane excitation through the specialized system less certain in the myocardium and smooth muscle. Whatever the detailed mechanism for the spread of excitation from the surface membrane into muscle fibers may be, it is generally accepted that the depolarization of the surface membrane releases or increases an activator in muscle cells which, in turn, triggers the contraction of actomyosin. The indications provided by several independent lines of inquiry show this activator to be calcium.

Evidence suggests that in heart muscle calcium ions are involved in the transmembrane current during the action potential. Although the mechanism involving the release of Ca^{++} upon excitation in muscles is unknown at present, it is generally agreed that binding of the released calcium to the actomyosin system initiates the contractile process. It is known now, that calcium-sensitive actomyosin system consists of at least four protein components: myosin, actin, tropomyosin, and troponin. Tropinin and tropomyosin are distributed along the entire thin filament of actin, and troponin appears to be a key protein through which the regula-

tory action of calcium is mediated to the contractile system. Troponin is bound to actin through tropomyosin, and the "tropomyosin-troponin" system inhibits the interaction of myosin and actin in the absence of calcium. Binding of calcium to the calcium-receptive protein, troponin, releases the inhibitory effect of these proteins on the interaction of actin and myosin, thus leading to activation of the contractile system. The above sequence of events leading to the final coupling of membrane excitation to the mechanical contraction necessitates the last step of the cycle, relaxation, namely, deactivation of the activator. It is generally agreed that the sarcoplasmic reticulum system is endowed with a powerful calcium transport mechanism which is capable of lowering the intracellular free calcium concentration below the threshold concentration. However, it is unknown at present to what degree the sarcoplasmic reticulum plays a role in the relaxation of smooth muscle.

Since calcium plays the central role in the current concept of excitation-contraction coupling, the calcium movement into the smooth muscle in the presence and absence of Panax Ginsen was investigated in the present study.

Another aspect of smooth muscle investigated in the present study is the effect of Panax Ginsen on the Na^+-K^+ activated ATPase of smooth muscle.

The discovery of Na^+-K^+ ATPase by Skou in 1957 laid the foundation for an enzymatic explanation of the sequence of events involved in the supply of energy for active sodium transport. It is now established that Na^+-K^+ ATPase is intimately identified with the active transport system of sodium from the heart muscle cells. It seems certain that the sarcolemma contains this Na^+-K^+ ATPase.

Thus the investigation is made on the effect of Panax Ginsen on the Na^+-K^+ ATPase of smooth muscle.

It was found that calcium movement into the aortic strip is inhibited in the presence of Panax Ginsen. This indicates that Panax Ginsen alters the membrane structure of smooth muscle cell and prevents calcium influx into the cell. This would result in less free calcium in the smooth muscle cell of blood vessels and interfere with the constriction of blood vessels. Thus the hypotensive effect of Panax Ginsen is probably due to its direct effect on the smooth muscle of blood vessels.

Panax Ginsen did not alter the N^+-K^+ ATPase indicating that membrane potential of smooth muscle is not altered in the presence of Panax Ginsen.

Therefore, it is conlcuded that Panax Ginsen interferes with the calcium influx phase of excitation-contraction coupling processes and inhibit the vasoconstriction resulting in the hypotensive response.