Electrophysiological Observations on the Digitalis-Potassium Interaction in Canine Purkinje Fibers

GARY J. ANDERSON, M.D., JOHN C. BAILEY, M.D., JOSEPH REISER, PH.D., AND ALAN FREEMAN, PH.D.

SUMMARY We studied the effects of elevating potassium concentration on the membrane potential of Purkinje cells exposed to toxic concentrations of acetylstrophanthidin or ouabain. Conventional intracellular microelectrode techniques were employed. Rapid elevation of [K+]o from 2.7 to 5.4 mEq/liter resulted in an initial increase (more negative) in membrane potential of cells demonstrating ouabain-induced phase 4 depolarization. The increase in maximal diastolic potential occurred initially without suppression of phase 4 depolarization. In cells rendered inexcitable by ouabain or acetylstrophanthidin, elevation of [K+]o consistently increased membrane potential and restored excitability. In four experiments automaticity was initiated within 2 minutes after the increase in [K+]o. Although automaticity reappeared, as maximal diastolic potential increased, the automatic rate slowed and then pacemaker activity was suppressed. Studies with 3H- ouabain showed that the increase in membrane potential paralleled K+-induced release of 3H-ouabain from Purkinje cells. These studies suggest that elevation of [K+]o reverses digitalis toxic manifestations in canine Purkinje fibers by causing release of cardiac glycosides bound to the membrane. The observed increase in membrane potential of ouabain-treated Purkinje fibers that occurred after [K+]o elevation was considered to be mediated in part by restoration of the Na pump and by electrogeneric pumping.

SINCE LOEWI 1 first suggested the use of potassium salts to suppress digitalis toxicity, the nature of the potassium-digitalis interaction has been a subject of intense and persistent interest. Observations on man 2 and animals 1, 3, 4, 5, 6, 7, 8 have established that K+ administration suppresses digitalis-induced arrhythmias and permits further administration of digitalis before the reappearance of arrhythmias. One of the mechanisms for this antiarrhythmic effect is suppression of automaticity, a well known effect of potassium. 10 Müller 11 reported in vitro studies demonstrating the electrophysiological consequences of the K+ interaction with digitalis poisoned Purkinje fibers. After an increase in extracellular potassium concentration ([K+]o) action potentials appeared more normal and were associated with improved rise times and overshoots, and there was an increase in the maximal diastolic potential. Polimeni and Vassalle 12 suggested that one mechanism for K+ suppression of ouabain-induced arrhythmias was an increase in potassium conductance. This was based, in part, on an earlier study 13 showing the elevation of [K+]o increased potassium conductance of pacemaker cells in the Purkinje system.

Our initial studies 14 showed that elevation of [K+]o overcame digitalis-induced block and was consistently associated with an increase in membrane potential that was independent of suppression of phase 4 depolarization. The purpose of this report is to describe our observations on the K+-digitalis interaction on canine Purkinje fibers.

Methods

Adult dogs weighing 10–20 kg were anesthetized with sodium secobarbital (30 mg/kg, iv). The heart was removed through a lateral thoracic incision and immediately placed...
in warm oxygenated Tyrode's solution. Single false tendons measuring 6–10 mm in length and 0.5–1.5 mm in diameter were obtained from the right ventricular endocardial surface. The false tendons then were placed in a 50-ml muscle chamber and continuously superfused with Tyrode's solution. The Tyrode's solution was gassed with 95% O2 and 5% CO2 in a 7-ml chamber and then flowed into the tissue chamber. The purpose of the first chamber was to prevent bubble formation in the tissue chamber. The Tyrode's solution contained, in mmol/liter, the following: NaCl, 137.0; KCl, 2.7; MgCl2, 0.5; NaH2PO4, 0.18; NaHCO3, 12.0; glucose, 5.5; and CaCl2, 2.7.

The rate of superfusion was 6 ml/min. The fluid level of the bath was maintained by constant overflow suction and the bath temperature was maintained at 37 ± 1°C. The pH of the solution was 7.1–7.3.

Glass microelectrodes having a tip diameter of less than 0.5 μm (15–30 MΩ resistance) were drawn from 1-mm Pyrex capillary tubing and filled with 3 M KCl. Tip potentials were <5 mV. Bipolar stimulating electrodes made of Teflon-coated stainless steel wires, bared at the tips, were applied to the Purkinje strand at its insertion into the endocardial surface of ventricular muscle and perpendicular to its long axis. The preparation was stimulated at a cycle length of 1 second. Stimuli were provided by an American Electronics Laboratories stimulus generator (model 104A). Conventional microelectrode techniques using capacitance neutralization were used as described in a previous communication.17 Data were recorded by Polaroid photography and were displayed on a Tektronix 564 memory oscilloscope with synchronization of the sweep generator (Tektronix 3B3) provided by the stimulus pulse generator. A Honeywell 7600 tape recorder and Visicorder were used for permanent data storage.

In each study, ouabain (2.1 x 10−7 m) or acetylstryphanthinidin (1.1 to 2.7 x 10−7 m) was administered until the monitored cells depolarized to −40 to −50 mV. On exposure to ouabain, phase 4 depolarization appeared initially and, with further exposure, automaticity supervened. As superfusion was continued automaticity disappeared and the cells ultimately became inexcitable regardless of stimulus duration or intensity. The bath concentration of potassium then was rapidly elevated from 2.7 to 5.4 mM/liter by bolus injection of potassium chloride into the 7 ml bubble chamber. Injection of the bolus of concentrated KCl into this chamber resulted in an initial dilution of the KCl prior to emptying into the larger (50-ml) tissue chamber. Mixing of the KCl to yield a final concentration of 5.4 mM/liter was assisted by interspersing plexiglass posts in the bath, thereby producing turbulent flow through the tissue chamber. Random sampling of [K+] in the 10-ml effluent of the tissue chamber was obtained at 30-second to 1-minute intervals to determine release of tritiated ouabain from the preparation. Tritiated ouabain was determined by conventional scintillation counting techniques.

Radioisotopic studies were performed to determine whether labeled ouabain (*H-ouabain, New England Nuclear, NET 211; specific activity, 13 Ci/mmol) was released in response to elevation of [K+]o. It was necessary therefore to design a protocol by which picomolar concentrations of ouabain could be detected isotopically. A three-chambered bath was constructed and consisted of an oxygenation chamber, a tissue chamber, and a mixing chamber. Tyrode's solution was oxygenated in a 4-ml chamber from which it flowed into the 10-ml tissue chamber. The tissue chamber effluent overflowed into a 10-ml sampling chamber containing wax-embedded plexiglass posts which mixed the Tyrode's solution. Prior to sampling, the contents of the sampling chamber was mixed. A 1-ml sample was withdrawn through a polyethylene tube for scintillation counting. Purkinje fibers initially were exposed to 1.8 x 10−7 m unlabeled ouabain and 0.2 x 10−7 m *H-ouabain (0.26 mCi/liter) until at least 10 mV of phase 4 depolarization was observed at a basic cycle length of 1,000 msec. It was assumed that part of the digitalis-induced electrophysiological changes were due to *H-ouabain. Since only picomolar changes in tissue content of *H-ouabain might be expected, the tissue bath would have to be relatively free of *H-ouabain except for that dissociating from the tissue. For this reason, after the onset of 10 mV of phase 4 depolarization, superfusion with the *H-ouabain was discontinued and Tyrode's solution containing nonlabeled ouabain (2.0 x 10−7 m) was perfused until inexcitability occurred. During the superfusion with nonlabeled ouabain the tissue bath solution was rapidly exchanged 16 times; this resulted in a final bath *H-ouabain activity of less than 600 disintegrations per minute per dpm.

Since small amounts of *H-ouabain still would be present in the bath at the time [K+]o was increased, continued superfusion with nonlabeled ouabain would further dilute *H-ouabain activity. To determine the dilution rate the tissue chamber was filled with nonlabeled ouabain sufficient to yield 600 dpm. Superfusion with nonlabeled ouabain was begun and samples of *H-ouabain were obtained from the sampling chamber at 1-minute intervals for scintillation counting. These data provided the dilution rate of *H-ouabain in the sampling chamber. This dilution rate was determined from the mean values obtained from five experiments and was identical to that calculated from flow rate and chamber volume. In the isotope studies bath [K+]o was elevated by bolus injection of potassium chloride and isotope samples were obtained at 30-second to 1-minute intervals to determine release of tritiated ouabain from the preparation. Tritiated ouabain was determined by conventional scintillation counting techniques.

**Results**

**EFFECTS OF ELEVATION OF [K+]O ON NORMAL PURKINJE CELLS**

In all of these studies, [K+]o was elevated from 2.7 mM/liter to 5.4 mM/liter in the course of the experiment. Since considerable emphasis is placed on changes in the resting potential, we studied the maximum diastolic potentials of cells exposed to normal Tyrode's solution (K+ = 2.7
THE EFFECTS OF ELEVATED [K+]o ON OUABAIN-INDUCED AUTOMATICITY

The purpose of these studies was to determine whether elevating [K+]o resulted in an increase in the maximal diastolic potential. Five experiments were performed in which Purkinje strands were exposed to ouabain until depolarization of phase 4, 15 mV/sec to 25 mV/sec, was observed. Figure 1 graphically illustrates results of one such experiment. In this experiment the preparation was superfused with ouabain for 59 minutes. At this time the cells demonstrated 6 mV of phase 4 depolarization. The maximal diastolic potential was −52 mV at the time the concentration of K+ was increased. The take-off potential (the membrane potential at the onset of phase 0) was −64 mV. The bath potassium concentration then was rapidly elevated from 2.7 to 5.4 mEq/liter. The initial effect of rapid elevation of [K+]o to 5.4 mEq/liter was an increase in the maximal diastolic potential to −55 mV while the take-off potential remained nearly unchanged. At 1 minute the take-off potential increased to −52 mV and this change was associated with a continued increase in maximal diastolic potential. Two minutes after elevation of [K+]o, suppression of phase 4 depolarization ensued and the take-off potential increased to −63 mV. At 140 seconds maximal diastolic potential was −65 mV and take-off potential was −63 mV. Thus, the degree of phase 4 depolarization initially increased as a result of an increase in maximal diastolic potential without change in take-off potential. This was followed by suppression of phase 4 depolarization, and increased take-off potential. Similar observations were recorded for all five experiments.

THE EFFECTS OF ELEVATED [K+]o ON OUABAIN-INDUCED DEPOLARIZATION OF RESTING PURKINJE CELLS

In 20 experiments Purkinje fibers were exposed to ouabain (2.1 × 10−3 M) in Tyrode’s solution containing potassium, 2.7 mEq/liter, until the tissue became inexcitable (mean −82.9 minutes). The stimulus then was discontinued and the tissue was allowed to remain quiescent in the bath for a period of 10 minutes. During this time no spontaneous electrical activity was observed, nor could action potentials be elicited by the application of electrical stimuli. There was no significant change (P > 0.5) in resting potential from the moment of inexcitability to the end of the 10-minute rest period during which time the resting potential was continuously monitored. After 10 minutes of quiescence the membrane potential was rapidly elevated and maintained at 5.4 mEq/liter. After elevation of the bath potassium concentration, an increase in the resting membrane potential was observed (Fig. 2). Mean control resting potential was −94.0 ± 5.0 mV and, with the development of inexcitability, the resting potential was −47.1 ± 4.3 mV. After elevation of potassium concentration, membrane potential stabilized by 4 minutes at −61.4 ± 4.1 mV. This membrane potential, once achieved, remained at the same level for periods in excess of 60 minutes, despite continued superfusion with ouabain.

FIGURE 1 After exposure to ouabain for 59 minutes, K+ concentration is elevated from 2.7 mEq/liter to 5.4 mEq/liter. Take-off potential was recorded as the membrane potential at which the action potential arose. Maximal diastolic potential represents the maximal negative potential recorded in the diastolic period. After elevation of [K+]o to 5.4 mEq/liter, maximum diastolic potential began to increase immediately without a change in take-off potential. At 140 seconds both take-off potential and maximal diastolic potential had stabilized at −63 mV and −65 mV, respectively.

FIGURE 2 Purkinje cells exposed to toxic concentrations of ouabain depolarize from a control resting membrane potential of −94 ± 5 mV to −47 mV after a mean exposure time of 82.8 minutes. The cells were then monitored for 10 minutes during which time no change in membrane potential occurred. Immediately prior to elevation of [K+]o (labeled Pre-K) mean membrane potential was −47 mV. [K+]o then was elevated from 2.7 mEq/liter to 5.4 mEq/liter; this was promptly followed by an increase in membrane potential from −47 mV to −60 mV after 4 minutes (see text).
THE EFFECTS OF ELEVATED \([K^+]_o\) ON ACETYLSTROPHANTHIDIN-INDUCED DEPOLARIZATION OF RESTING PURKINJE CELLS

Twenty-five experiments were performed to determine the response of cells exposed to acetylstrophanthidin and subsequently to an elevation of \([K^+]_o\). Mean control resting potential was \(-87.3 \pm 2.4\) mV. The mean time of exposure to acetylstrophanthidin required to cause inexcitability was 50.4 minutes. At this time the average resting potential was \(-46.3 \pm 5.6\) mV. The bath concentration of \(K^+\) then was rapidly elevated to 5.4 mEq/liter and maintained at this level by raising the \([K^+]_o\) of the acetylstrophanthidin-Tyrode's solution to 5.4 mEq/liter. An increase in membrane potential began within 1 minute after elevation of \([K^+]_o\). By 4 minutes hyperpolarization was maximal at \(-60.0 \pm 1.2\) mV. The membrane potential remained stable at this level for periods similar to that observed with ouabain. This time course of recovery was identical to that observed with ouabain.

POTASSIUM-PRECIPITATED AUTOMATICITY

In four experiments the elevation of \([K^+]_o\) after exposure to ouabain resulted in the development of automaticity in previously inexcitable cells. Purkinje preparations were exposed to ouabain until the tissue became inexcitable or no longer demonstrated automaticity. The bath \([K^+]_o\) then was rapidly elevated following the protocol described above, with the subsequent development of automaticity. One example of this is shown in Figure 3 and graphically illustrated in Figure 4. Action potentials from two Purkinje cells were recorded from a false tendon and are displayed in Figure 3. After exposure for 70 minutes to ouabain the cells depolarized to \(-35\) mV and \(-45\) mV, respectively. The membrane potential was monitored for 10 minutes and during this time there was no change in membrane potential. The bath \([K^+]_o\) then was elevated from 2.7 mEq/liter to 5.4 mEq/liter by bolus injection of KCl and maintained at 5.4 mEq/liter by superfusion with Tyrode's solution containing 5.4 mEq/liter \(K^+\) and ouabain. Figure 3 shows the potentials recorded 2.4 minutes after elevation of \([K^+]_o\). Membrane potential had increased by 5 mV in one cell and by 17 mV in the other when automaticity occurred. The first action potential is seen in the bottom trace of the upper panel and resembles a pacemaker potential. Phase 4 depolarization was recorded from both cells with the action potential of one cell (bottom trace) preceding the other (top trace) although the latter appears to be recorded from the area of the pacemaker. There was a gradual slowing of the rate of discharge associated with suppression of the phase 4 depolarization (bottom panel) until the cells became quiescent again. After elevation of \([K^+]_o\) and prior to the onset of automaticity one cell repolarized to \(-41\) mV and the other to \(-63\) mV (Fig. 4). With the development of automaticity both cells depolarized minimally and then further hyperpolarization ensued. On cessation of automaticity the cells demonstrated resting potential of \(-47\) mV and \(-67\) mV, respectively.

INTERACTION BETWEEN \(K^+\) AND \(^{3}H\)-OUABAIN BINDING

Five studies were performed to determine whether elevation of \([K^+]_o\) affected binding of \(^{3}H\)-ouabain to Purkinje membranes. In these studies the tissue was exposed to \(^{3}H\)-ouabain (see Methods) until the development of phase 4 depolarization was observed. Once phase 4 depolarization was observed, the tissue bath was flushed with 16 exchanges of nonlabeled ouabain in a similar concentration. The nonlabeled ouabain was superfused until the onset of

![Figure 3](attachment://image.png)

**Figure 3** Action potentials recorded from two Purkinje cells in a false tendon after exposure to ouabain sufficient to induce inexcitability. \(K^+\) concentration then was elevated from 2.7 to 5.4 mEq/liter. The action potentials shown occurred spontaneously 2.4 minutes after elevation of \([K^+]_o\). The membrane potential progressively became more negative and the automatic rate gradually slowed over 45 seconds until the cells became quiescent again.
Figure 4 Graphic representation of resting potential and maximal diastolic potential (during automaticity) of action potentials shown in Figure 3.

inexcitability. Samples for $^{3}$H-ouabain then were obtained immediately prior to elevation of $[K^{+}]_{o}$. These data are shown in Figure 5. The mean $^{3}$H count prior to elevation of $[K^{+}]_{o}$ was 435 dpm. The bath $[K^{+}]_{o}$ was then rapidly elevated to 5.4 mEq/liter and maintained by constant superfusion of Tyrode's solution containing a similar concentration of nonlabeled ouabain. One minute after elevation of $[K^{+}]_{o}$ the $^{3}$H-ouabain count had risen to a mean value of 585 dpm. This initial increase in $^{3}$H-ouabain count was observed in four of five experiments and averaged 34.5%. The maximal increase in $^{3}$H-ouabain concentration observed was 140%. In one experiment no increase in $^{3}$H-ouabain was observed but the count remained above the dilution curve for the bath. The mean value for the control isotope count is indicated by the open circle. At 1 minute the open circle indicates the expected value derived from the dilution curve for the isotope (see Methods). After the initial increase, $^{3}$H-ouabain activity decayed and was not significantly different ($r = 0.9756$) from the dilution curve (Fig. 6).

Discussion

The data reported in this paper illustrate several effects of raising extracellular potassium concentration on Purkinje fibers exposed to toxic concentrations of acetylstrophanthidin or ouabain. These are: (1) an increase in membrane potential independent of suppression of phase 4 depolarization; (2) restoration of excitability concomitant with the increase in membrane potential; (3) release of previously bound $^{3}$H-ouabain; and (4) suppression of phase 4 depolarization. It was interesting to note that the sequence of events leading to glycoside toxicity was reversed. That is, in the Purkinje preparations exposed to cardiac glycosides, we noted the following sequence: "normal" → phase 4 depolarization → reduction of maximal diastolic potential → automaticity → continued loss of maximal diastolic potential → inexcitability. After elevation of $[K^{+}]_{o}$ we observed the reversal of this sequence although the preparation did not return completely to the control state, suggesting that mechanisms other than suppression of toxic manifestations were operative. The term reversal, then, implies that cardiac glycosides were being released from the membrane binding sites, as opposed to suppression, which implies that the toxic manifestations would recur if $K^{+}$ concentration were returned to normal. This is supported by the observation that $[K^{+}]_{o}$ elevation precipitated automaticity and then, over a period of 30 seconds, suppressed automaticity. This suggested to us that $K^{+}$ initially reverted the Purkinje cell to a "less toxic" state, i.e., demonstrating automaticity rather than inexcitability.

The finding of an increase in membrane potential of Purkinje fibers exposed to acetylstrophanthidin or ouabain...
in response to elevation of [K\(^+\)]\(_o\) was not an unexpected finding. Müller\(^{14}\) showed that elevation of [K\(^+\)]\(_o\) from 2.7 to 5.4 mEq/liter increased the membrane potential of ouabain-depolarized Purkinje cells by 5 mV. Müller conjectured that an increase in intracellular potassium concentration ([K\(^+\)]\(_i\)) might account for this observation. An increase in [K\(^+\)]\(_i\), occurring subsequent to elevation of [K\(^+\)]\(_o\), has been reported for various experimental conditions.\(^{18},^{22}\)

Such an increase in [K\(^+\)]\(_i\) might be mediated via Na\(^+\), K\(^-\)-ATPase activity.\(^{29}\) Na\(^+\), K\(^-\)-ATPase activity is known to be inhibited by cardiac glycosides.\(^{31}\) Potassium has several effects on this interaction, including a reduction in the rate of digitalis-ATPase binding\(^{12},^{13}\) and a reversal of Na\(^+\), K\(^-\)-ATPase inhibition by ouabain.\(^{25},^{26}\) An increase in [K\(^+\)]\(_i\), would be expected after elevation of [K\(^+\)]\(_o\), if the reversal of Na\(^+\), K\(^-\)-ATPase inhibition induced by K\(^+\) resulted in an increase in Na\(^+\), K\(^-\)-ATPase pump activity. The data presented in Figures 4 and 5 supported the second of these observations, in that \(^{3}H\)-ouabain activity in the effluent significantly (P < 0.01) increased after elevation of [K\(^+\)]\(_o\). Thus, the release of glycoside would tend to restore pump activity and thereby would favor restoration of a higher [K\(^+\)]\(_i\). The noted increase in \(^{3}H\)-ouabain activity, however, does not quantitatively accurately the relative amount of glycoside released. The initial increase in \(^{3}H\)-ouabain may be mediated by several factors. The slope of this line is related to exchange of the tissue \(^{3}H\)-ouabain with the surrounding medium, in which different exchange rates are a function of the total \(^{3}H\)-ouabain bound and the magnitude of the exposed surface area. The contribution of these factors to experimental variation could be minimized to some degree in this experimental design by employing comparable tissue sizes and exposures. However, the slope of the lines above the dilution curve after 1 minute are difficult to ascribe to any given factor. On the other hand, the increase in \(^{3}H\)-ouabain within 1 minute after elevation of [K\(^+\)]\(_o\) cannot be accounted for other than by K\(^-\)-mediated release of bound \(^{3}H\)-ouabain.

The finding of release of \(^{3}H\)-ouabain in response to elevated [K\(^+\)]\(_o\), is not in agreement with published data\(^{44}\) for experiments in vivo. Animals made hyperkalemic (6.5 to 7.8 mEq/liter) after digoxin administration did not show significant differences in myocardial glycosid levels from controls. However, these authors pointed out that the minute amounts that may have been released were too small to be detected by currently available techniques for measuring tissue levels. Since the amount released in our studies was measurable in picomolar concentrations, it would be unlikely that such quantities could be measured in the tissue samples studies for preparations in vivo.

The observed increase in membrane potential after elevation of [K\(^+\)]\(_o\), also may be accounted for in part by electrogenic sodium pumping. An electrogenic sodium pump has been suggested for both nerve\(^{27},^{28}\) and cardiac\(^{29},^{30}\) tissue. The electrogenic sodium pump has been shown to be activated by either increased [K\(^+\)]\(_o\) or [Na\(^+\)]\(_o\) and reduced in activity by decreasing [K\(^+\)]\(_o\).\(^{33},^{34}\) Recent studies on strophanthidin-treated nerve have suggested that the potassium-induced hyperpolarization similar to that shown in this report is due to electrogenic pumping.\(^{33}\) This would not be unexpected in light of our experimental protocol, which favors an increased electrogenic contribution for three reasons: (1) the glycoside increases [Na\(^+\)]\(_o\); (2) [K\(^+\)]\(_o\) is increased from 2.7 to 5.4 mEq/liter; and (3) glycosides are released from membrane binding sites (Figs. 5 and 6) and potentially increase the number of active pumping sites. The time course of the hyperpolarization following potassium administration (Fig. 2) also is sufficiently rapid to suggest some component of electrogenic pumping, since [K\(^+\)]\(_o\) would not likely increase at the rate required to account for the observed hyperpolarization.

A third alternative for the observed increase in membrane potential is an increase in potassium conductance (G\(_K\)) as proposed by Vassalle\(^{1}^{9}\) and Müller.\(^{14}\) Kassebaum\(^{1}^{*}\) and Muñoz and Trautwein\(^{17}\) have shown that cardiac glycosides increase conductance in a way similar to that caused by potassium alone.\(^ {35}\) It might be assumed that the increase in [K\(^+\)]\(_o\), may further increase G\(_K\) and induce hyperpolarization. Further studies, however, are necessary to establish this mechanism.

Our observation that an increase in [K\(^+\)]\(_o\), could precipitate automaticity (Fig. 4) was perplexing. Two explanations for this observation were considered. First, we noted that K\(^+\) administration was associated with a release of cardiac glycoside from the tissue. This would result in the return of the tissue to a "less toxic" state, i.e., one in which the tissue shows evidence of automaticity rather than inexcitability. The second possible explanation for the development of automaticity relates to the effect of cardiac glycoside release from membrane binding sites. Since G\(_K\) is increased by glycoside binding to the membrane,\(^ {36},^{37}\) it is reasonable to assume that release of cardiac glycosides results in a decrease in G\(_K\). Furthermore, on the basis of our data demonstrating that ouabain is released by elevation of [K\(^+\)]\(_o\), (Fig. 5), a decrease in G\(_K\) would be expected. Moreover, Geduldig\(^{48}\) postulated an inverse relationship between conductance and pump activity, in that G\(_K\) increased with decreasing sodium pump rates. Part of this hypothesis was based on the theory that the channels available for passive diffusion were located at sodium pump sites. Thus, when pump activity ceased, passive diffusion would be maximal. If K\(^+\) elevation releases ouabain from binding sites, a concomitant decrease in G\(_K\) would ensue as more sites become available for pump activity. This would favor the induction of automaticity. However, the finding of eventual suppression of automaticity (Figs. 3 and 4) is inconsistent with this hypothesis unless very rapid changes in conductance are occurring in some complex interrelationship with electrogenic pumping and changes in [K\(^+\)]\(_o\).

It should be emphasized that the data reported in this study were derived from Purkinje preparations in a late stage of digitalis intoxication. Our observations on the digitalis-potassium interaction do not necessarily imply that similar data might be observed at earlier stages of intoxication.

References


K+-DIGITALIS INTERACTION

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