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COMPARATIVE STUDY ON THE ELECTROPHYSIOLOGICAL EFFECTS OF MONENSIN ON ATRIAL AND VENTRICULAR MUSCLE PREPARATIONS OF GUINEA-PIG HEART

Ahmed Fahmy, Nabila El-Maraghy, Atef El-Gharabawy, Mohamed Abd El-Aal and Herman Nawrath*

Dept. of Pharmacology, Faculty of Pharmacy, Zagazig University, Egypt
**Dept. of Pharmacology, Faculty of Medicine, University of Mainz -Germany*

ABSTRACT

The effects of monensin (10 μmol/L) alone and in presence of verapamil (3 μmol/L) or ouabuin (1 μmol/L) or glibenclamide (10 μmol/L) or $BaCl_2$ separately were studied on the electrophysiological properties represented by force of contraction, duration of action potential, and membrane resting potential of isolated atrial and ventricular muscle of guinea -pig heart. Monensin induced a transient increase in the force of contraction of atrial and ventricular muscles. It caused a decrease in action potential duration of papillary muscle, this effect was reversed by glibenclamide. Monensin increased the action potential duration of atrial muscle in absence or presence of glibenclamide. In presence of ouabain monensin induced a significant depolarization of resting membrane potential in both atrial and ventricular muscles. Verapanil did not antagonize the effects monensin. Monensin induced an increase in Na^+, a transient increase in Ca^{2+} and a decrease in K^+ contents of atrial and ventricular tissues. From the data of the present work it could be concluded that, Na^+ pumped out the cell by Na^+/K^+ pump was less in atria then in ventricles in presence of moninsin. Less consumption of intracellular ATP in ventricular cells than in atrial cells, thus the ATP of ventricular cells did not reach the critical concentration level which open ATP dependent K^+ channels. The study also showed absence of Na^+ dependent K^+channels in guinea-pig atria.

INTRODUCTION

In most regions of mammalian heart, the upstroke of the action potentials is produced by an influx of Na^+ through the sodium channels. Thus, sodium ions are important for excitation and conduction in heart muscle[1]. In cardiac tissues, there are, two types of sodium channels namly fast sodium channels and slow sodium channels[2].

Obviously, there are more than single class of calcium channels in cardiac cells[3]. Evidently, cardiac cells at rest are mainly K-selective, so that the membrane potential is largly governed by the K^+ equilibrium potential[4]. Recently, different types of K channels were identified in cardiac tissues, e.g. ATP-dependent-K channels, voltage and time dependent K-channels[5-7].

Monensin transports sodium ion mainly and to less extent potassium ion, down their concentration gradient across biological membranes[8].

The aim of the present study was to compare the electrophysiological effects of monensin alone and in presence of verapamil or ouabain or glibenclamide and $BaCl_2$ on the atrial and ventricular muscle preparations of guinea-pig heart.

EXPERIMENTAL

1- Preparations:

Guinea-pigs of weights 250/400g were sacrificed by a blow to the head and bled from the carotid arteries. Suitable right ventricular, papillary muscles or trabeculae were isolated by ligating both ends with a fire suture and dissecting them from the heart. Right artial trabeculae from guinea-pigs were prepared in the same way.

2- Solutions:

The Tyrod's solution had the following composition in mM/L: Na Cl 136.9; KCl 54; $MgCl_2$ 1.05; Na_2PO_4 0.42; Na HCO_3 11.9; $CaCl_2$ 1.8; glucose 5.6. The solution was equilibrated with 5% CO_2 in O_2 of 37° C. (pH 7.4).

3- Measurement of tensions and transmembrane potential :

Guinea-pig heart preparations were electrically stimulated to contract at 1 Hz by rectangular pulses of 0.1 to 1 msec.

Duration of 10% above the threshold intensity using a Grass stimulator (models 4) and isolation unit. Force of contraction was recorded isometrically. The preparation were allowed to stabilize for at least 45 min. The effects of drugs were investigated be exposure to either single or to cumulatively increasing concentrations, achieved by adding drugs to main Tyrode's reservoir and increasing the concentrations after the establishment of a stable response. The transmembrane potential was defected intracellularly by the use of 10 to 20 Mohm glass microelectrodes filled with 3 mol/L of KCl. Both transmembrane potential and tensions were displayed on an oscilloscope (Nicolet 310) and stored on discs for further evaluations.

4- Measurement of $^{86}Rb^+$ efflux :

Whole guinea-pig left atria were first exposed to about 10 Meq. $^{86}Rb^+$ for 90 min in Tyrode's solution and then transferred into the test baths. The preparations were kept at rest. The release of $^{86}Rb^+$ into non radioactive Tyrode's solution was then followed for 30 min.

Under control conditions and 15 min in the presence of monensin (10 μmol/L). The bath solution was changed every 5 min and collected in scintillation

vials for later determination of radioactivity. At the end of experiment, radioactivity of atrial preparation and those of solutions were determined by liquid scintillation counter (Tricarb 3380, Packard Instrument, Frankfurt).

5- Determination of tissue electrolytes :

The electrolyte contents (Na^+, K^+, Ca^{2+}) of atria and ventricles were determined according to **Langer *et al.*, 1967**. Samples of atria or ventricles were weighed and dried at 105°C. in hot over for 36 hr and was ashed at 600°C in muffle furnace. The ash was then dissolved in bidistilled water and used for determination of Na^+, K^+ or Ca_2^+ contents using specific Kit for each ion.

6- Drugs : The following drugs were used (sources in parentheses):

Atenolol (Sigma, Deisenhofen, FRG); verapamil (Knoll, Ludwigshafen, FRG); ouabain (Serva, Heidelherg, FRG); glibenclamide (Sigma, Deisenhofen, FRG); ^{86}Rubidium chloride (NEN, Dreieich, FRG).

7- Evaluation of results and statistical analysis :

Results are either demonstrated as original figures or expressed as mean ± standard error of means (SEM). Action potential recordings were analyzed for maximal upstroke velocity (dv/dtmax), and duration (APA) at 20% and 90% of depolarization , APD_{20} and APD_{90}, respectively. Changes of the RP in the hyperpolarizing direction one described as an increase and in the depolarizing direction as a decrease in the RP. A single rate constant of $^{86}Rb^+$ efflux could be determined according to $\lambda = (Ln\ A_0 - Ln\ A_0 / t)$ derived from $A = A_0^{e-\lambda t}$. Statistically significant differences were assessed by Student's t-test or by analysis of variance[10] allowed by modified t-statistic according to **Dunnett, C.W. (1964)**[11].

RESULTS

1- Effect of monensin (10 μ mol/L) on the force of contraction and action potential in guinea-pig heart muscle preparations:

As shown in Fig.(1), monensin (10 μ mol/L) induced a transient increase in force of contraction in both atrial and ventricular muscle preparations. No change in resting tension was noticed during whole period of experiment. At the same time, monensin induced a significant decrease in the action potential duration in ventricular muscle that in atrial muscle was significantly increased.

The effect of monensin on other action potential parameters in both atrial and ventricular muscle preparations are summarized in table (1).

2- Effect of cumulative addition of monensin on action potential parameters in atrial and ventricular muscle preparations of guinea-pig heart:

Cumulative addition of increasing concentrations of monensin induced a concentration- and time-dependent increase in APD in atrial muscle and a decrease in APD in ventricular muscle as shown in Fig. (2).

Table (2) summarizes the other effects of cumulative addition of monensin on the action potential parameters of guinea-pig heart muscle preparations.

3- Effect of monensin (10 μmol/L) on membrane resting potential (either) in the presence of $BaCl_2$ or ouabain:

Under control conditions, a hyperpolarizing effect of a drug on the membrane RP may be hardly detectable, because the value is already near the equilibrium potential for potassium. Therefore the influence of monensin on the membrane resting potential was determined in the presence of $BaCl_2$.

Figure (3) shows the original records of the membrane RP under control conditions; after the addition of $BaCl_2$ (0.4 μ mol/L and 0.2 μ mol/L) for papillary and atrial muscle respectively. The membrane RP was decreased from -87 mV. to -77 mV. and -84 mV to -53 mV for ventricles and atrial muscle, respectively. Further addition of monensin (10 μ mol/L induced an increase of membrane RP for -77 to -86 mV and from -53 mV to -71 mV for papillary and atrial muscle, respectively.

Figure (4) summarizes the results obtained with monensin (10 μ mol/L) on membrane RP of atrial and ventricular muscles in the presence of $BaCl_2$. We have shown so far that monensin (10 μ mol/L) increases the membrane RP of guinea pig heart muscle preparations under normal conditions (Table 1) and in the presence of $BaCl_2$.

Figure (5) shows the original records of the membrane RP under control after the addition of ouabain (4 μ mol/L and 2 μ mol/L) for papillary and atrial muscle, respectively. The membrane RP was decreased from -85 mV to - 80 mV for both papillary and atrial muscles; further addition of monensin (10 μ mol/L) decreases the membrane RP to -73 mV and -71 mV for papillary and atrial muscles, respectively.

A summary of the changes in membrane RP induced by monensin (10 μ mol/L) in the presence of ouabain on papillary and atrial muscles, preparations are shown in Figure (6).

(4) Effect of glibenclamide on action potential in the presence of monensin :

As shown in Fig (7), addition of monensin (10 μ mol/L) caused a decrease of APD_{90} from 210 to 120 ms. Under these conditions, further addition of glibenclamide, (10 μ mol/L) induced partial reversal of ADP from 120 ms to 183 ms.

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Figure (8) presents summary of seven experiments. Monensin (10 μmol/L) caused a significant shortening of APD_{90} from 203 ± 4 ms to 112 ± 15 ms ($p < 0.05$). Under these conditions, further addition of glibenclamide (10 μ mol/L) induced a partial reversal but significant of APD_{90} from 112 ± 15 ms to 166 ± 8 ms ($p < 0.05$).

Other changes in action potential parameters induced by the addition of monensin and glibenclamide are summarized in Table (3).

(5) Effect of cumulative addition of monensin on action potential duration in Guinea-pig papillary muscle in the presence of glibenclamide:

After stabilization of the papillary muscle preparations addition of glibenclamide (10 μ mol/l) did not induce significant effects on action potential parameters.The shortening of the APD in guinea-pig ventricle induced by cumulative increasing concentrations of monensin in the presence of glibenclamide is less than in its absence, Fig (9) and table (4).

(6) Effect of monensin on the force of contraction and AP in guinea-pig atria in the presence of verapamil (3μ mol/L):

As shown in Fig (10) and represented in Table (5), verapamil (3m mol/L) induced a significant decrease of APD_{20} ($p < 0.05$), while APD_{90}, RP, and maximal upstroke velocity 9dv/dtmax) were not significantly changed. Force of contraction was significantly reduced (28 ± 2% of control). Under these conditions, further addition of monensin (10μ mol/L) induced a significant increase of force of contraction (265 ± 27 % of control). APD_{90} was significantly increased from 82 ± 3 to 95 ± 3 ms, membrane RP was significantly increased from -84.3 ± 1 mV to -87±102 mV. On the other hand, APA, APD_{20} and maximal upstroke velocity 9dv/dtmax) were not significantly changed upon the addition of monensin.

7- Effect of monensin (10 μ mol /L) on $^{86}Rb^+$ efflux in guinea-pig atria:

Figure (11) shows the influence of monensin (10 μ mol/L) on $^{86}Rb^+$ efflux in guinea-pig atrial muscles. Exposure of the muscles to normal Tyrode's solution containing atrial (10 μ mol /L) and DMSO 1% v/v for 30 min did not affect $^{86}Rb^+$ efflux of the muscles. Further exposure of the muscles to monensin (10 μmol/L) for 15 min had no significant effect on $^{86}Rb^+$ efflux.

8- Effect of monensin (10 μ mol/L) on electrolyte changes in tissues of guinea-pig atrium and ventricle:

As shown in Figure (12a,b) in both atrial and ventricular tissue monensin induced an increase in Na^+ content while it induced a decrease in K^+ content. Ca^{2+} tissue content increased after 20 min and then decline to the normal values after 80 min.

DISCUSSION

In the present study, monensin induced positive inotropic effect followed by a decrease in developed force in guinea pig atria and ventricular preparations. These effects could support a previous results obtained from different isolated heart muscle preparations e.g. canine ventricular muscle[12] isolated ventricular myocytes from dog and rabbit[13], guinea pig atria[14].

Since it was reported that the induced alteration of cardiac contractile force reflect a change in free myoplasmic Ca^{2+} concentration[15], we studied the effect of monensin on the ventricular muscle. Our results showed an increase in sodium content and a transient increase in the cell calcium content of both preparations. The observed transient increase in tissue calcium concentrations and consequently transient increase in force of contraction could be due to one or more of the following mechanisms:

a) Monensin facilitate Na^+-H^+ exchange across cardiac cell membrane[8] the effect which may lead to increased capacity of phosphatidylserene to bind[16] with Ca^{2+}.

b) Increased H^+- in and Ca^{2+}- out exchange[17].

c)Monensin decreased the a mount of ATP inside the cell[18,19]. This in turn may cause a decrease in Ca^{2+} current.

Moreover, in the present study verapamil was not able to abolish the inotropic effect of monensin and consequently exclude the role of Ca^{2+} channels from the transient increase in tissue Ca^{2+} content. By using Fura-2 technique, **Ertl *et al*** [20] found that monensin induced a transient increase in free myoplasmic Ca^{2+} concentration in guinea - pig atrial and ventricular myocytes.

Also, results in the present study showed that monensin induced a significant increase in resting membrane potential either under normal conditions or in the presence of $BaCl_2$. This effect in agreement with previous results obtained by **Horackova, 1986**[21] who demonstrated that, monensin caused hyperpolarization in cardiac myocytes of dog and rabbit.

The majority of the observed hyperpolarization in the present study is due to stimulation of Na/K pump. This proposal is supported by, our results which showed that a Rb efflux was not changed 15 min after the addition of monensin.

d) Monensin induced depolarization in guinea - pig ventricular and atrial muscle preparations in the presence of ouabain.

Furthermore, the present study by using guinea - pig papillary muscle demonstrates that monensin induced a significant shortening of APD

Table (1): Effect of monensin (10 µmol/L) on action potential in guinea-pig heart muscle preparations. The muscles were superfused with normal Tyrode's solution containing atenolol (10 µmol/L) and electrically stimulated at 1 Hz.

	atrial muscle		papillary muscle	
	control	moensin	control	monensin
RP (mV)	-85±0.6	-87*±1	-85±0.05	-88±0.05*
ADP (mV)	112±1	114±1	121±1	120±1
ADP_{20} (ms)	14±1	17*±1	94±8	40±8*
APD_{90} (ms)	70±3	84±4*	204±3	105±12*
dV/dt_{max} (V/s)	241±27	224±20	231±6	224±7

Values are absolute means ±S.E.M. * Significant difference ($P<0.05$)
RP, resting potential; APA, action ptential amplitude; ADP_{20}, action potential duration at 20% of repolarization; dV/dt_{max}, maximal upstroke velocity.

Table (2): Effect of cumulative addition of increasing concentrations of monensin on action potential in guinea-pig heart muscle preparations. The muscles were superfused with normal tyrode's solution containing atenolol (10µmol/L) and electrically stimulated at 1Hz.

	Control	Monensin (1µmol/L)	Monensin (3µmol/L)	Monensin (10µmol/L)
RP (mV) (atria)	-85.3±0.5	-87*±0.5	-87*±0.5	-87*±0.5
RP (mV) (ventricle)	-86±1	-87.6*±1	-88.6±1	-88.2±1
APA (mV) (atria)	15±1	117±1	116±1	115±2
ventricle	120±1	119±1	116*±2	110*±2
ADP_{20} (ms)(atria)	13±3	17*±3	16*±2	16*±2
ventricle	81±4	62*±7	15*±2	7*±1
dV/dt_{max} (V/S) (atria)	263±19	280±30	272±27	252±30
(ventricle)	260±15	259±16	251±25	230±27

Values are absolute means ±s.e.m. (n=7)
* significant difference from control ($P<0.05$)
RP, resting potential; APA, action petential amplitude; ADP_{20}, action petential duration at 20% of repolarization: dV/dt_{max} maximal upstroke velocity.

Table (3): Effect of glibenclamide (10µmol/L) on action potential in guinea pig papillary muscles in the presence of monensin (10µmol/L) The muscles were superfused with normal Tyrode's solution containing atenolol (10µmol/L) and electrically stimulated at 1 Hz.

	Control	Monensin (10µmol/L)	Glibenclamide (10µmol/L)
RP (mV)	-85.3±0.4	-88*±0.5	-88*±1
APA (mV)	121±1	119±1	118±2
ADP_{20}(ms)	88±9	42*±10	66**±9
dV/dtmax (V/S)	237±6	229±8	233±13

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Table (4): Effect of cumulative addition of increasing concentrations of monensin on action potential duration at 90% of repolarization in guinea-pig papillary muscles in the presence or absence of glibenclamide (10µmol/L). The muscles were superfused with normal Tyrode's solution containing atenolol (10µmol/L) and electrically stimulated at 1Hz.

	Control	Monensin (1µmol/L)	Monensin (3µmol/L)	Monensin (10µmol/L)
Monensin	189±6	151±6	65±7	37±4
Monensin (in the presence of (glibenclamide)	201±15	176±17	139*±15	114*±14

Values are absolute means±S.E.M.
* Significant difference from monensin without glibenclamide ($P<0.05$)

Table (5): Effect of monensin (10µmol/L) on action potential parameters in guinea-pig atrial muscles in the presence of verapamil (3µmol/L). The atrial muscle preparations were superfused with normal Tyrode's solution and electrically stimulated at 1Hz.

	Control	Monensin (3µmol/L)	Glibenclamide (10µmol/L)
RP (mV)	-84.3±1	-84.6±1.2	-87*±1.2
APA (mV)	114±0.5	114.5±0.5	115±1.0
ADP_{20}(ms)	18±1	11.5*±1	105.±0.5
dV/dt_{max} (V/S)	242±26	227±26	241±27

Values are absolute means ±s.e.m. (n=3)
* significant difference from control ($P<0.05$)
RP, resting potential; APA, action petential amplitude; ADP_{20}, action petential duration at 20% of repolarization; dV/dt_{max} maximal upstroke velocity.

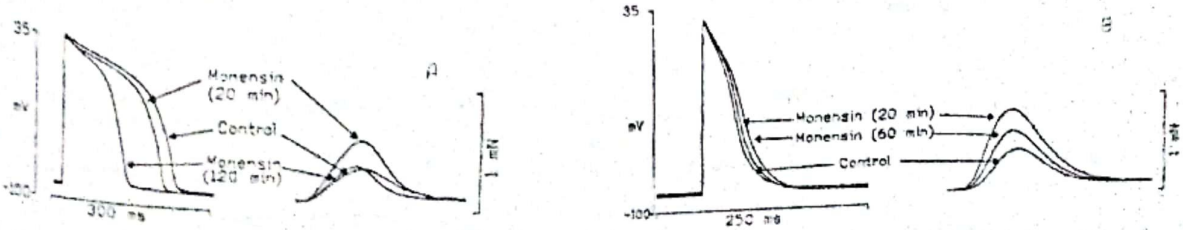

Fig. (1): Original records showing the effect of monensin (10 µmol/L) on force of contraction (right traces) and action potential (left traces) in guinea-pig papillary muscle (A) and atrial muscle (B) in the presence of atenolol (10 µmol/L).

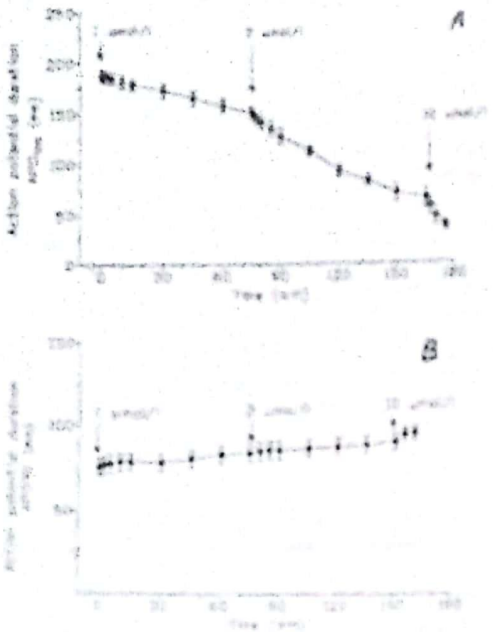

Fig. (2). Time course of the effect of cumulative addition of increasing concentrations of ouabain on action potential duration (APD_{90}) in guinea-pig papillary muscle (A) and atrial muscle (B) in presence of acetylcholine (10 μmol/L).

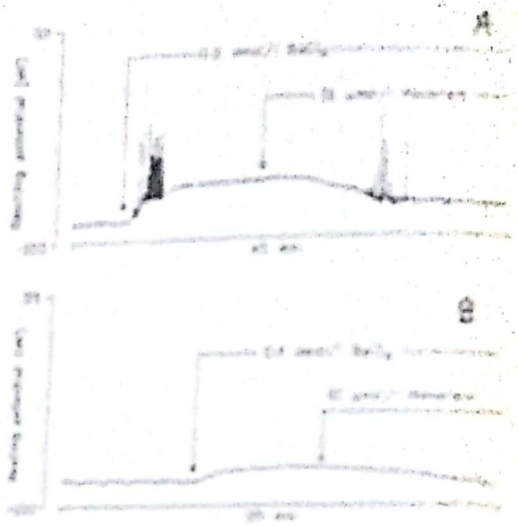

Fig. (3). Original record showing influence of acetylcholine (10 x 10^{-6} mol/L) on resting potential in a quiescent guinea-pig left ventricular (A) and papillary muscle (B) in presence of ouabain.

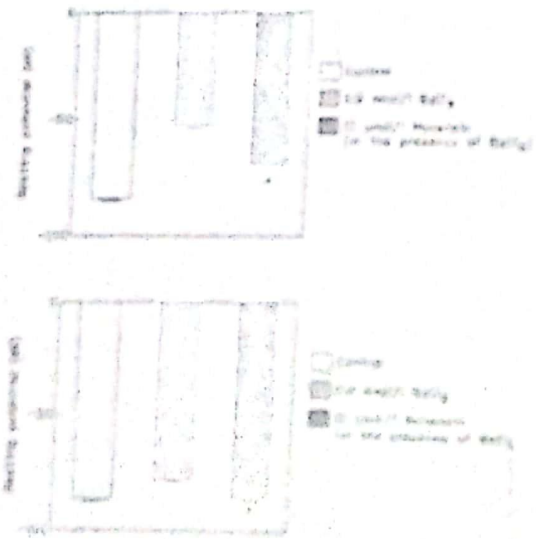

Fig. (4). Influence of acetylcholine (10 μmol/L) on resting potential in quiescent guinea-pig papillary muscle (A) and atrial muscle (B) in the presence of barium.

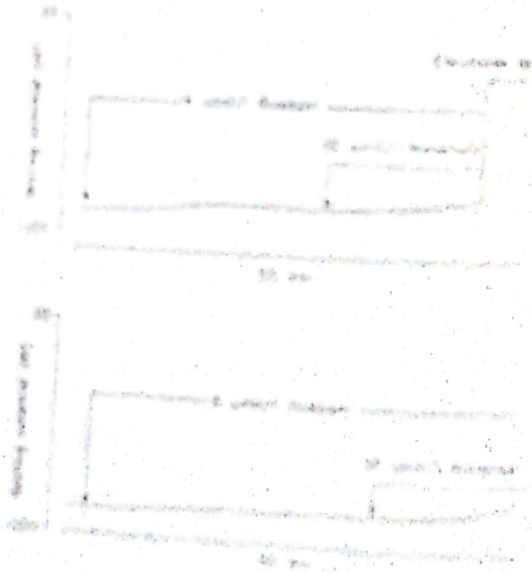

Fig. (5). Original record showing the influence of acetylcholine (10 x 10^{-6} mol/L) on resting potential in a quiescent guinea-pig left ventricular (A) and papillary muscle (B) in presence of ouabain.

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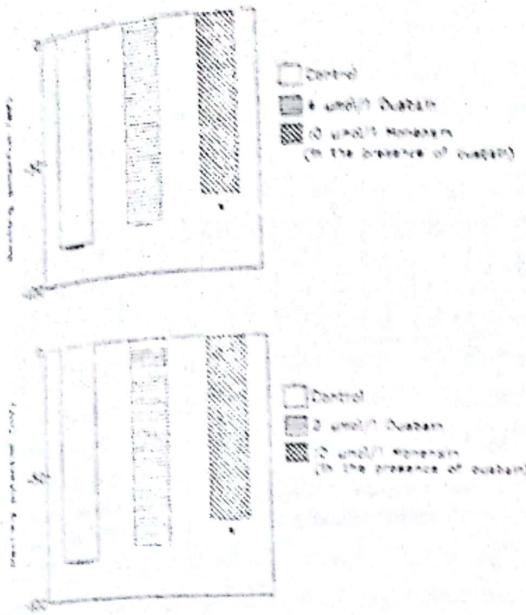

Fig (6): Influence of monensin (10 μmol/L) on resting potential of quiescent guinea-pig papillary (A) of atrial (B) muscles in the presence of ouabain. The muscles were superfused with normal Tyrode's solution containing atenolol (10 μmol/L). Data are shown as mean ± SEM. Ouabain caused a decrease in resting potential. Under this condition, further addition of monensin induced more and (*)significant decrease in resting potential ($P < 0.05$).

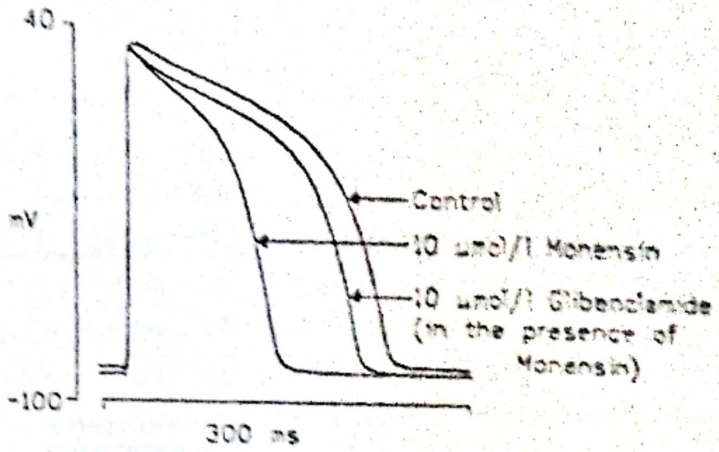

Fig (7): Original records showing the effect of glibenclamide (10 μmol/L) on action potential duration in guinea-pig papillary muscle in the presence of monensin (10 μ mol/L). The papillary muscle was superfused with normal Tyrode's solution containing atenolol (10 μ mol/L) and electrically stimulated at 1 Hz. Addition of monensin caused a decrease in action potential duration. Further addition of glibenclamide induced prolongation of action potential duration.

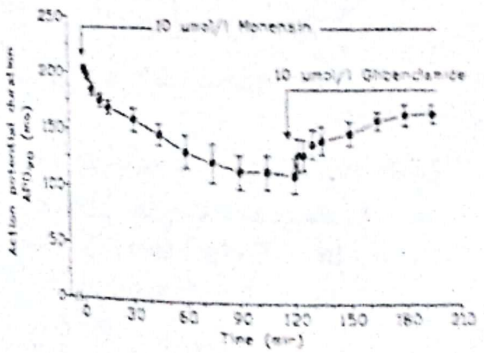

Fig (8): Effect of glibenclamide (10 μ mol/L) on action potential duration of guinea-pig papillary muscles in the presence of monensin (10 μ mol/L) and atenolol (10 μ mol/L). The papillary muscles were superfused with normal Tyrodes solution and electrically stimulated at 1 Hz. Ordinate represent absolute values of action potential duration (APD_{90}) in ms. Data are shown as mean ± S.E.M. of six experiments. 120 min after the addition of monensin, action potential duration was markedly shortened. Further addition of glibenclamide partially reversed the effect of monensin on action potential duration.

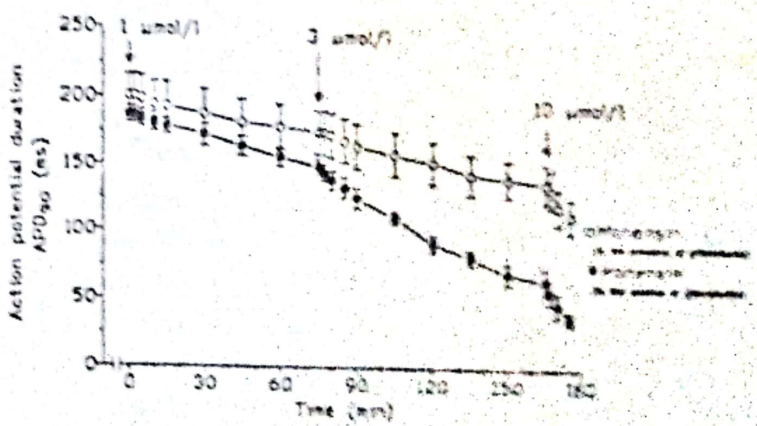

Fig (9): Time course of the effect of cumulative addition of increasing concentrations of monensin on action potential duration (APD_{90}) of guinea-pig papillary muscles, both in absence (closed circles) and presence (open circles) of glibenclamide (10 μmol/L). The papillary muscles were superfused with normal Tyrodes solution containing atenolol (10 μ mol/L) and electrically stimulated at 1 Hz. Arrows indicate addition of monensin. Ordinate represents absolute values of action potential duration (APD_{90}) in ms. Data are shown as mean ± S.E.M. of three experiments in the presence of glibenclamide and six experiments in the absence of glibenclamide. Note that the presence of glibenclamide reduced the effect of monensin on action potential duration (APD_{90}).

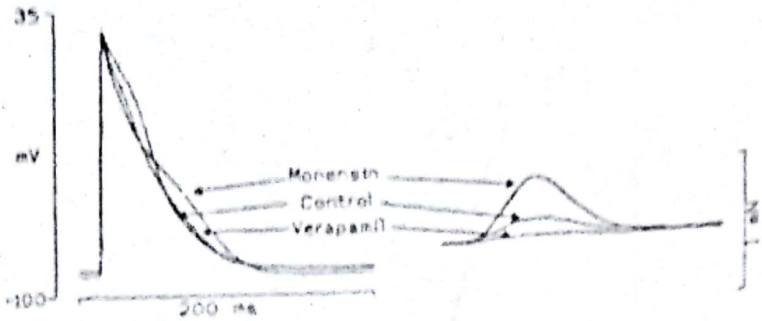

Fig. (10): Original records showing the effect of monensin (10 μ mol/L) on force of contraction (right ventricular action potential (left traces)) in guinea-pig left atrium in the presence of atenolol (10 μmol/L) and verapamil (3 μmol/L). The atrial muscle preparation was superfused with normal Tyrode's solution and electrically stimulated at 1 Hz. Addition of verapamil evoked a decreased of force of contraction and very slight prolongation of action potential duration (APD_{90}). Further addition of monensin induced increased in force of contraction and pronounced prolongation of action potential duration (APD_{90}).

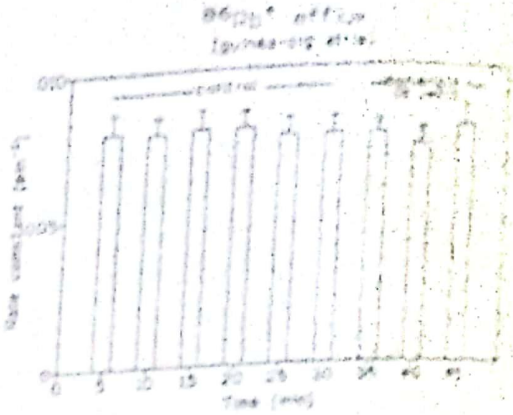

Fig. (11): Influence of monensin (10μ mol/L) on ^{45}Ca efflux in guinea-pig atria in normal Tyrode's solution containing atenolol (10μ mol/L). Data shown as mean ± S.E.M. (n =8).

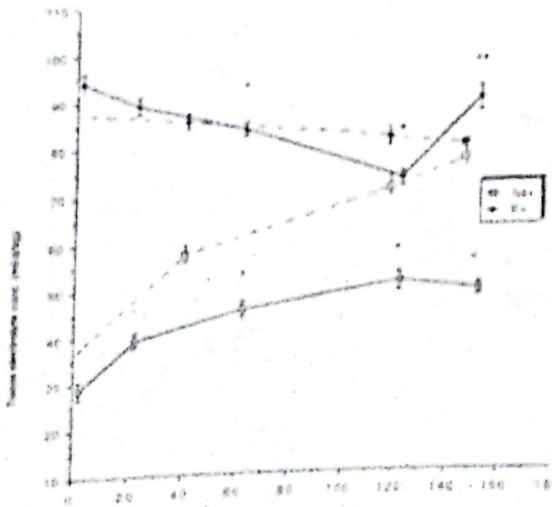

Fig. (12a): Changes in tissue Sodium and Potassium content of guinea-pig atrium (▲) ventricle (○) produced by monensin (10 μ mol/L) in normal Tyrode's solution containing atenolol (10 μ mol/L).
Each point represents mean ± S.E.M. of six preparations.
*Significantly different from control ($P<0.05$).
**Significantly different from effect of monensin alone ($P<0.05$).

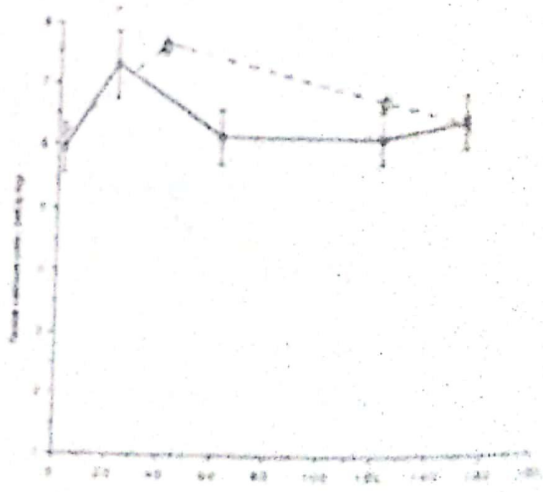

Fig.(12b): Changes in tissue Calcium content of guinea pig atrium (▲) ventricle (○) produced by monensin (10 μ mol/L) in normal Tyrodes solution containing atenolol (10 μ mol/L).
Each point represents mean ± S.E.M. of six preparations.
*Significantly different from control ($P<0.05$).

Glibenclamide reduced the effect of monensin on APD. Also, the addition of glibenclamide induced partial reversal of the shortened action potential duration induced by monensin.

Since it was reported that glibenclamide can block ATP-dependent K^+ channels[22], the observed shortening of action potential duration by monensin in the present study may be in part, due to stimulation of ATP-dependent K channels.

Our study demonstrated that, monensin induced a significant increase of APD in guinea-pig atrial muscle preparation. This effect is not due to increase of slow inword current carried by Ca^{2+} since it was not blocked by verapamil. Furthermore, this increase in APD is not due to increase of slow sodium current (Window current), since **Jacob & Newrath, 1988)**[23] found that TTX had no effect on APD in guinea pig atria. Thus the observed increase in PAD could be due to :

1- Induction of creep content[24].

2- Guinea pig atria contains less scale Na^+-K^+ ATP as than in ventricle[25].

a) Therefore, more accumulation of Na^+ inside the cell incur the effect of monensin.

b) Less consumption of ATP, these ATP did not reach the critical concentration level which open ATP dependent K^+ channels.

c) The presence of Na^+-dependent K^+ channels in atria have not reported yet.

From the data of the present study it could be concluded that:

(1) Na^+ pumped out of the cell by Na^+/K^+ pump is less in atria than in ventricles i.e. more accumulation of Na^+ inside the cell under the effect of monensin which may lead to prolongation of action potential's.

(2) Less consumption of intracellular ATP in ventricular cells thus ATP have not reached to the critical concentrations level which open ATP dependent K^+ channels.

(3) Absence of Na^+ dependent K^+ channels in guinea - pig atria.

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دراسة مقارنة للتأثيرات الفسيولوجية الكهربية للمونفسين على عضلات الأذين والبطين المفصولة من قلب خنزير غينيا

أحمد فهمى - نبيلة المراغى - عاطف الفرباوى - محمد عبد العال - هيرمان نفرات*

قسم الفارماكولوجى - كلية الصيدلة - جامعة الزقازيق - مصر.

*قسم الفارماكولوجى - كلية الطب - جامعة ماينز بألمانيا.

فى هذا البحث تمت دراسة مقارنة للتأثيرات الفسيولوجية الكهربية لعقار المونفسين على العضلات المفصولة من كل من الأذين والبطين فى خنزير غينيا، وذلك للمونفسين منفرداً أو فى وجود كلوريد الباريوم، والأوابين والجلايبنكلاميد والفيراباميل.

وقد أظهرت النتائج أن عقار المونفسين يؤدى إلى زيادة مؤقتة فى قوة انقباض العضلات فى الأذين والبطين. وكذلك يؤدى إلى زيادة طول زمن فاعلية الجهد للخلية فى الأذين وتقصير هذا الزمن فى البطين. وتؤدى إضافة الجلايبنكلاميد إلى انعكاس تأثير المونفسين على زمن فاعلية الجهد فى البطين.

يؤدى المونفسين إلى زيادة الجهد الكهربى للخلية فى كل من الأذين والبطين هذا التأثير فى وجود كلوريد الباريوم وقد وجد أن الأوابين يعكس هذا التأثير.

كما وجد أن عقار المونفسين يؤدى إلى زيادة فى كمية أيونات الصوديوم والكالسيوم بينما يحدث انخفاض فى كمية البوتاسيوم فى أنسجة كلا من الأذين والبطين.

من خلال نتائج البحث يمكن استنتاج أن

عقار المونفسين يؤدى إلى تراكم الصوديوم فى خلايا الأذين بدرجة أكبر من البطين ويؤدى ذلك إلى زيادة فى طول زمن فاعلية الجهد. فى خلايا البطين يقل استهلاك ثلاثى فوسفات (ATP) الأدينوزين وبالتالى لايصل إلى الحد تفتح عنده قنوات البوتاسيوم المعتمدة عليه. غياب قنوات البوتاسيوم المعتمدة على الصوديوم فى أذين خنزير غينيا.