

Assessment of Albendazole (antiparasitic drug) effects on the physiological activities of the cardiac, smooth and skeletal muscles of some experimental animals.

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ABSTRACT

Albendazole (ABZ) is a broad-spectrum antihelminthic for the treatment of intestinal helminth infections. It also has anti-hydatid activity and is recognized to have important application in treatment of human cystic and alveolar echinococcosis as well as some cases of cardiac echinococcosis. The first target of this study is to monitor and assess the changes in the ECG parameters of the rat during the first 24 hours after treatment with ABZ. Another *in vitro* investigations are conducted to evaluate the effect and the mode of action of ABZ on the contractile properties of the skeletal muscle and the smooth muscles of the gut. The effect of oral administration of Albendazole (400-mg/kg. Body weight) on the heart rate (HR) and ECG parameters (P-R and Q-T interval, R and T waves amplitude) was investigated. Although the HR started to fall after 6 hours, a significant bradycardia was only recorded after 12 and 18 hours. This negative chronotropic effect was concomitant with a non-significant prolongation in the P-R interval at the same time points. A gradual elevation in the R-wave amplitude with a significant difference only after 9 and 12 hours compared to the control values was recorded. On the other hand, the Q-T interval and T-wave amplitude showed mild non-significant changes during the whole time course. It can be concluded that the main effect on the cardiac muscles might be induced by the oxidation reactions of the drug and its metabolite, however, it is mild and transient changes. To confirm this postulation, we monitored the serum levels of creatinine phosphokinase (CPK). Values of CPK started to increase significantly after 3 hours and reached its maximum level after 24 hours then started to decline to almost the control measures by the end of the time course (192 hours). The experiments performed on the isolated rabbit's duodenum revealed a stimulatory effect of ABZ and nicotine blocks this presser effect. On the other hand, atropine failed to prevent the stimulatory action of Albendazole. These results indicated that the effect of ABZ on the isolated smooth muscle of the gut is mediated through the parasympathetic

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ganglia. ABZ decreased the mechanical activity of the skeletal muscle fibers. This inhibitory action could be related to a depolarizing blocking effect, since addition of neostigmine (anticholinesterase drug) to the medium failed to reverse the effect of the drug.

More detailed investigations should be done on the pharmacodynamics of the drug especially on the cardiovascular system to confirm its safety. Also, it is important to emphasize that care should be taken in case of using Albendazole in the treatment of patients suffering from heart diseases.

KEYWORDS: Albendazole, ECG, CPK, Skeletal muscles, Smooth muscles.

INTRODUCTION

Albendazole (Methyl 5-propylthio-1 H-benzimidazole-2-YL carbamate) is a broad-spectrum anthelmintic for the treatment of intestinal helminth infections. It also has anti-hydatid activity and is recognized to have important application in treatment of human cystic and alveolar echinococcosis (Saimot *et al.* 1983; Davis *et al.* 1986; Horton 1989; Todorov *et al.* 1992; Wen *et al.* 1994).

Marriner and Bogan (1980) reported that Albendazole is a potent member of the benzimidazole (BZS) group of anthelmintics, with wide range of activity against gastrointestinal roundworms including inhibited larval stages, tapeworms, liver flukes, and lung worms in many species. They found that much of the anthelmintic activity of Albendazole in sheep is due to the metabolically formed sulfoxide (ABZ-SO) and sulfone (ABZ-SO₂). Albendazole blocks glucose uptake in the larval and adult stages of susceptible parasites, thereby depleting the energy stores and decreasing formation of ATP leading to immobilization and death of the parasite (Bertram 1992).

Following oral administration, Albendazole is rapidly absorbed and can not be detected in plasma, because the drug is quickly metabolized in liver mainly to Albendazole sulfoxide and to a lesser extent, to other metabolites (Marriner *et al.* 1986). About 3 hours after a 400-mg oral dose, the sulfoxide attains its maximum plasma concentration. The metabolites are mainly excreted in the urine and only a small amount is excreted in the faeces (Bertram, 1992). Albendazole is absorbed to a much greater degree than the other BZS because 47% of the administered dose is recovered in urine over a 9-day period (Prichard & Henessy, 1981).

Adults and children more than two years of age take Albendazole as a single oral dose (400 mg). In children, Albendazole appears superior to mebendazole for curing hookworm infections and reducing egg counts (Albonico *et al.* 1994). There are some evidence that this dose induces mild cytotoxic effects in the liver of the rat during the first 4 days following oral administration of the drug (Abd El-Rahman *et al.* 1999). Sir (1991) mentioned that Albendazole induced some blocking action on the autonomic ganglia in dogs. Some changes in cardiovascular parameters were observed in dogs receiving 1 mg/kg Albendazole intravenously, which were maximal at 30 min but returned to normal after 1 hour.

In spite of being used recently in the treatment of cases of cardiac echinococcosis (Ozdemir *et al.* 1997; Vicol *et al.* 1998), no detailed studies on the effect of ABZ on the electrical activity of the cardiac muscles (ECG), have been conducted.

The first target of this study is to monitor and assess the changes in the ECG parameters during the first 24 hours after oral administration of ABZ into rats. Another *in vitro* investigations are conducted to evaluate the effect and the mode of action of ABZ on the contractile properties of the skeletal muscle since it is used now in the treatment of the peripheral muscular hydatidosis (Carpintero 1997). Also, the same kind of investigation have been performed on the smooth muscles of the gut because it is the main pathway of ABZ absorption and more importantly that ABZ is biotransformed partly to ABZ-SO by the gut (Lawrenz *et al.* 1992).

MATERIALS AND METHODS

Effect of ABZ on the cardiac muscles

Experimental animals

Males Sprague Dawley rats (100-150 gm) were used in this study. All rats were kept under hygienic conditions where food and water were allowed *ad-libitum*. Two groups of animals were used for this experiment (5 rats/group). The first one treated with Albendazole (400 mg) orally using gastric tube and the second group administered the vehicle (distilled water) and considered as a control group.

ECG recording

ECG was recorded according to the method described by Buschmann *et al.* (1980) by using bipolar lead II electrodes in the direction of the heart axis as advised by Sporri (1944). Animals were i.p. Anaesthetized with urethane (1.25 gm/kg b.wt) and kept in thermoregulated chamber ($27^{\circ}\text{C} \pm 2.0$) during the whole recording time. Rats were fixed in supine position and prepared for implantation of ECG electrodes. Three electrodes were subcutaneously implanted in the sites of recording where one electrode was put at the right side of the neck and the other one under the right thigh while the third electrode was inserted beneath the caudal end of the sternum and served as a reference. Following implantation, electrodes were connected to a combined heart rate coupler (FC 127), which is attached to the MD2 Oscillograph (Life Science Products, Bio-science, UK). The paper speeds used were 25 and 50 mm/sec and the wave voltage was calibrated after a stabilization period for at least 30-min before application of the drug to serve as self control for each animal. Heart rate (HR) and different ECG parameters (P-R & Q-T intervals and R- & T-wave amplitudes) were recorded after 3, 6, 9, 12, 18 and 24 hour from treatment for both groups (drug-treated and control).

The heart rate (HR) was measured and calculated from R-R interval (Budden *et al.* 1980) in beats/min from the ECG records at a paper speed of 50 mm/sec as follows:
$$\text{HR (beat/min)} = \text{Paper speed (50)} \times 1 \text{ min (60 sec)} / \text{distance between two consecutive R-waves in mm.}$$

The P-R interval was measured from the beginning of the P wave to the onset of the QRS complex while Q-T interval is measured from the start of the QRS to the highest point of the T wave. Heering (1970) defined the termination of the T waves as the point at which it becomes horizontal or at this, which the next P wave begins considering the liability of the T wave of rat's ECG.

The amplitude of both R and T waves were measured from the isoelectric line up to the highest point of each wave in mV. The point at which P-wave terminates and the QRS complex begins that was considered the point of isoelectric line (Beinfeld & Lehr 1968).

Measurement of creatinine phosphokinase (CPK)

In order to assess that the recorded changes in the ECG could be related to a direct effect of ABZ on the myocytes, CPK activities were monitored in the sera of the treated and control rats. It is well known that CPK present in high concentration in the myocardium and damaged cells leak this enzyme into circulation. Blood samples were collected from the same animals used for the ECG recording after 3, 6, 12, 24, 48, 96 and 192 hours post-treatment using orbital sinus technique (Sanford 1954). To obtain serum, the collected blood was incubated at room temperature for one hour, then centrifuged at 3000 rpm for 20 min in a cooling centrifuge. The sera were aspirated and stored at -20°C until used for the measurement of the activities of creatinine phosphokinase (CPK) using Biomerieux kits (Laboratory reagent and instrument, France) and UV-Visible spectrophotometer (Shimadzu-1601-PC, Japan).

Effect of ABZ on smooth and skeletal muscles

Experimental animals

Four adult male rabbits (*Oryctolagus cuniculus*) weighing about $1.7 \text{ kg} \pm 7$ were used to study the effect of ABZ on the isolated smooth muscle (duodenum). A total of 12 mature toads (*Bufo regularis*) were prepared for the isolation of gastrocnemius muscle sciatic nerve preparation to evaluate the effect and the mechanism of Albendazole action on the skeletal muscles.

Chemicals

Albendazole was a kind gift from Pfizer Egypt Company as 1.9 % suspension (Valbazen). Atropine sulphate was obtained from Misr Company (Egypt) and Nicotine was purchased from Aldrich (Gillingham, UK), while Neostigmine and all other chemicals were bought from Sigma (St. Louis, USA). The physiological salt solutions (Tyrode's and Frog's Ringer) were prepared as indicated by Chapman *et al.* (1979)

Isolated smooth muscle preparation

This experiment was undertaken to study the effect of Albendazole on smooth muscle (rabbit's duodenum) using the method of Chapman *et al.* (1979). Rabbits were slaughtered and the abdomen was opened. A length of about 3-cm strips of the first part of small intestine was taken and suspended in aerated Tyrode's solution in 50 ml capacity organ bath (No ME 15808, 220 Volts, 50 HZ, Inco. Ambola, India) at 37°C. Tracings were recorded on different speeds of C.F. Palmer kymograph (B. Brawn, Melsungen AG, type 861062, No 1799, V 220. A 0.01, HZ 50, W. Germany) with smoked drum paper using a frontal writing lever. ABZ was added to the bath in different concentrations (1%, 2%, 3%, 5%, 7.5% and 10%) and the maximum effect was recorded after the addition of the 5% dose. The preparation was washed twice after each dose and allowed to rest for at least 5-min between each treatment. Nicotine (1%) and atropine sulphate (4 ug/ml) were used to study the mode of action of ABZ on the smooth muscle.

Skeletal muscle preparation

The method described by Chapman *et al.* (1979) was used for studying the effect of Albendazole on the gastrocnemius muscle sciatic nerve preparation of the toad. Animals were pithed and the skin around all the body was removed. Achilles tendon was cut at the distal portion of gastrocnemius muscle. The lower leg was removed just below the knee

joint. The sciatic nerve was located and freed from the surrounding muscles. The complete nerve muscle preparation was mounted in frog Ringer's solution at room temperature. Activity of the skeletal muscle was recorded by using an ink kymograph (10500, Bioscience, UK) with paper speed 1mm/sec. Sciatic nerve was stimulated with 1V for 1.4-msec at 1hz square pulse waves. ABZ (5% solution) was perfused directly to the muscle to study its effect on the mechanical contractions. An anticholinesterase drug, neostigmine (100 ug/ml), was used to investigate the mechanism of action of ABZ.

Statistical analysis

Values of the HR, different ECG parameters and CPK for both drug-treated and control animals were represented as means \pm S.E. Student's unpaired *t*-test was performed for analysis of the data according to Snedecor (1956). Group differences were considered statistically significant at the level of $P < 0.05$.

RESULTS

Effect of ABZ on the cardiac muscles

The effect of oral administration of Albendazole (400 mg/kg. b.wt) on the normal electrical activity of the myocardium, heart rate and ECG parameters (P-R and Q-T interval, R and T waves amplitude) was investigated.

Figure (1) and plate (1) show the effect of Albendazole on the heart rate of anaesthetized rats. Although the HR started to fall after 6 hours, there was no significant difference in its values compared to the control values at all times except after 12 and 18 hours where there was a significant bradycardia.

P-R interval represents the conduction time of impulse through the atrioventricular node. The comparison between treated and control groups showed that the conduction time was increased non-significantly after 12 and 18 hours in the ABZ treated rats and returned back to control levels after 24 hours (Figure 2A and Plate 1).

The time between the onset of ventricular excitation to the end of ventricular repolarization is represented by Q-T interval in the ECG traces. Although there was an increase in the Q-T interval, the data indicated that the drug did not produce any significant change during the recording time (Figure 2B and Plate 1).

The effect of Albendazole on the R-wave amplitude, which represents the ventricular depolarization is illustrated in Figure (3A) and Plate (1). It was noticed that there was a significant increase in the force of the ventricular contractility only after 9 and 12 hours from Albendazole administration as compared to their control groups. On the other hand, the R-wave amplitude increased non-significantly at the other time points.

The amplitude of the T-wave (ventricular repolarization) was among the tested parameters in the ECG of the rat after drug administration. Figure (3B) and Plate (1) demonstrates the effect of Albendazole on the T-wave amplitude. The drug did not produce any significant effect on the ventricular repolarization phase during the whole experimental time course as compared to the control values.

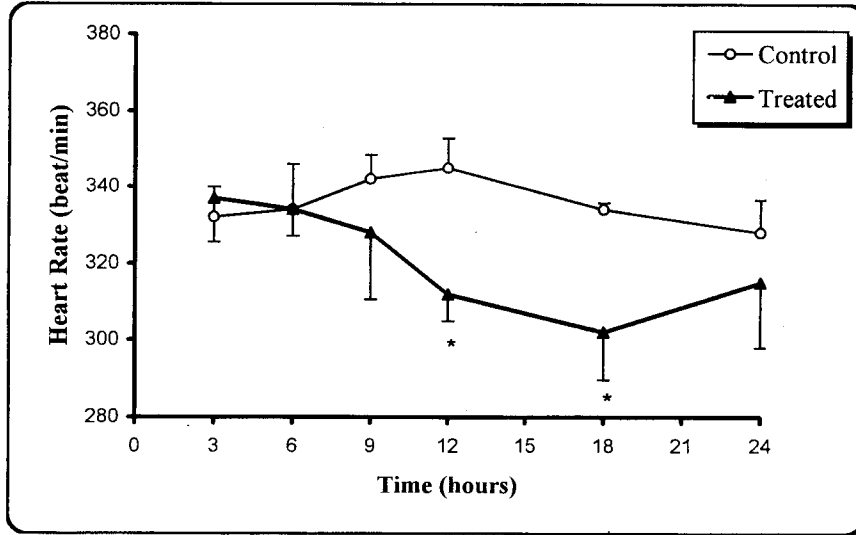


Figure (1): Effect of oral administration of Albendazole (400 mg/kg) on the heart rate (HR) of urethane anaesthetized rats. Vertical bars represents mean \pm SE of 5 rats/group. Control animals injected orally with the vehicle (distilled water). * Significantly different compared to the control group, Unpaired t-test ($P < 0.05$).

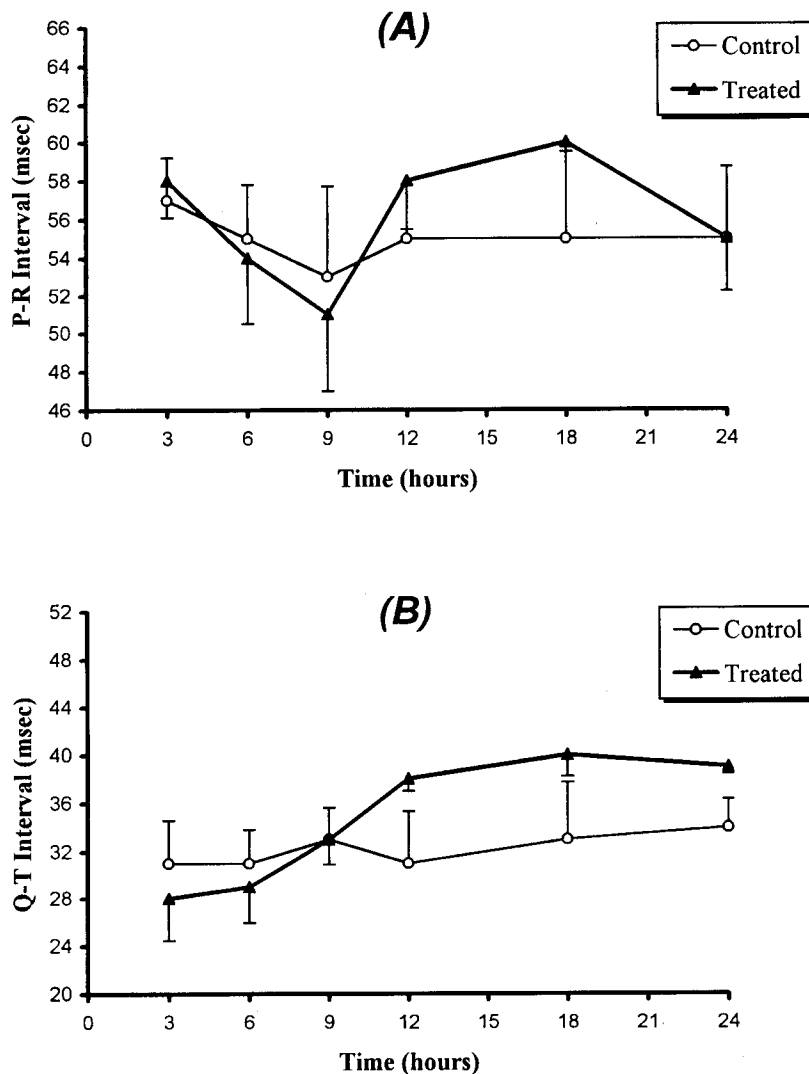


Figure (2): (A) Effect of oral administration of Albendazole (400 mg/kg) on the P-R interval of urethane anaesthetized rats. (B) Effect of oral administration of Albendazole (400 mg/kg) on the Q-T interval of urethane anaesthetized rats. For further explanation, see Fig. (1).

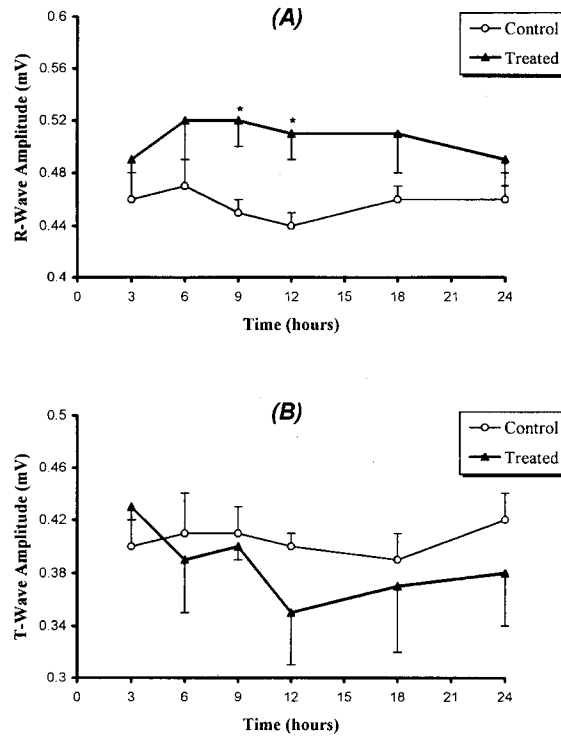


Figure (3): (A) Effect of oral administration of Albendazole (400 mg/kg) on the R-wave amplitude of urethane anaesthetized rats. (B) Effect of oral administration of Albendazole (400 mg/kg) on the T-wave amplitude of urethane anaesthetized rats. For further explanation, see Fig. (1).

PLATE (1)

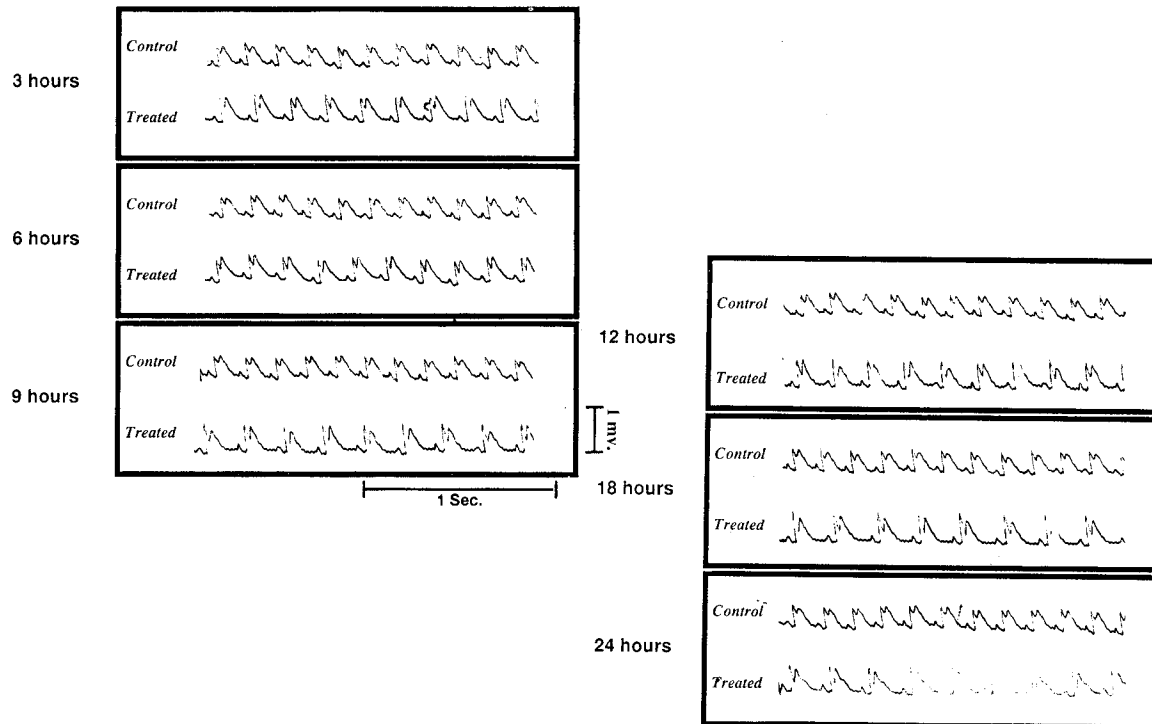


Plate (1): ECG traces showing the effect of oral administration of Albendazole (400 mg/kg) on the heart rate (HR), P-R & Q-T intervals as well as R- & T-wave amplitudes of urethane anaesthetized rats. ECG was monitored for 24 hours and recorded at the indicated time points from drug treated and control animals (5 rats/group). Paper speed was 50 mm/sec.

Serum creatinine phosphokinase (CPK)

Serum CPK levels were monitored for 8 days in the treated and control animals used in the ECG study to assess the severity of the damage that might occur to the myocytes. The activity of CPK was significantly increased in Albendazole treated rats as compared to their control animals at 3, 6, 12, 24 and 48 hours. On the other hand, the elevated values of CPK declined with time and nearly reached to the control level after 192 hours (Figure 4).

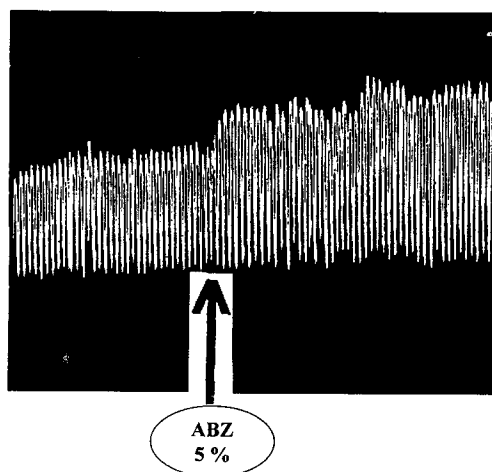


Figure (4): Effect of oral administration of Albendazole (400 mg/kg) on the serum creatinine phosphokinase (CPK) of rats. For further explanation, see Fig. (1).

Effect of Albendazole on the isolated smooth muscles

The effect of Albendazole on the rabbit's duodenum was studied. Addition of different concentrations of Albendazole (1%, 2%, 3%, 5%, 7.5% and 10%) produced a stimulatory effect on the intestinal motility of duodenum and the highest contraction level was induced by ABZ dose of 5% (Plate 2). An attempt was made to investigate the site of action of Albendazole on the smooth muscle where the probability of ganglionic stimulation by Albendazole was tested by blocking the intestinal autonomic ganglia with nicotine sulphate (1%). Addition of Albendazole (5%) did not produce its stimulatory effect. This indicates that the effects of Albendazole might be mediated through ganglionic interaction between the drug and the smooth muscle ganglia (Plate 3A). The cholinergic effect was tested by addition of Albendazole 5% to the rabbit's duodenum after blocking the muscarinic receptors with atropine sulphate (4 μ g/ml). Although the stimulatory effect of ABZ on the smooth muscle seems to be delayed in the presence of atropine, the later couldn't prevent the pressor effect of Albendazole (Plate 3B).

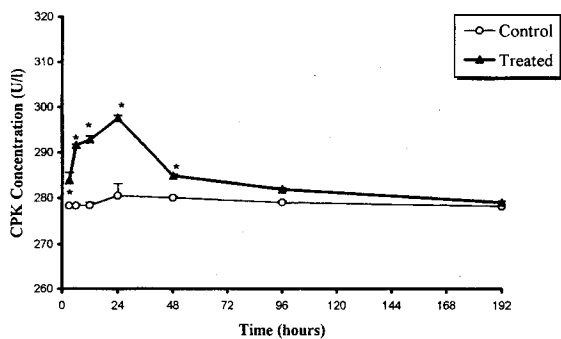


Plate (2): Representative trace for the contractile effects of ABZ (5%) on the smooth muscles. Strips from rabbit's duodenum were immersed in 50 ml aerated Tyrode's solution at 37 °C during the recording time.

PLATE (3)

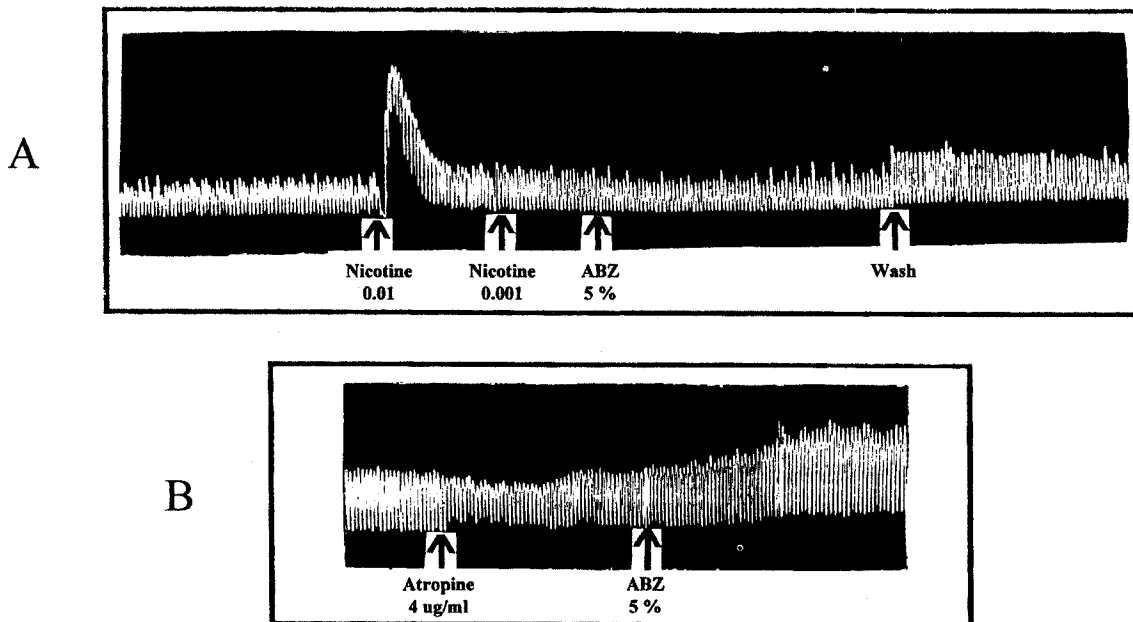


Plate (3): Representative trace for the contractile effects of ABZ (5%) on the smooth muscles. Strips from rabbit's duodenum were immersed in 50 ml aerated Tyrode's solution at 37 °C during the recording time.

(A) Notice that addition of nicotine (ganglionic blocker) before ABZ (5%) prevents the stimulatory effect of the drug.

(B) Notice that using atropine (4 ug/ml) prior to the ABZ (5%) treatment did not abolish the pressor action

Effect of Albendazole on the skeletal muscles

The normal rhythmic contraction of the gastrocnemius-sciatic nerve preparation of the toad to a square pulse wave of 9 volts / 5 second interval were recorded. Plate (4A) demonstrates the effect of perfusion of the gastrocnemius muscle with Albendazole (5%). The application of the drug decreased the muscle contraction. In this investigation we used an anticholinesterase drug, neostigmine, to study the mechanism of ABZ action on the skeletal muscles. Administration of neostigmine (100 µg/ml) alone stimulate the skeletal muscle preparation (Plate 4B), while its addition after the treatment with the drug (5%) enhance the inhibitory effect of Albendazole (Plate 4C).

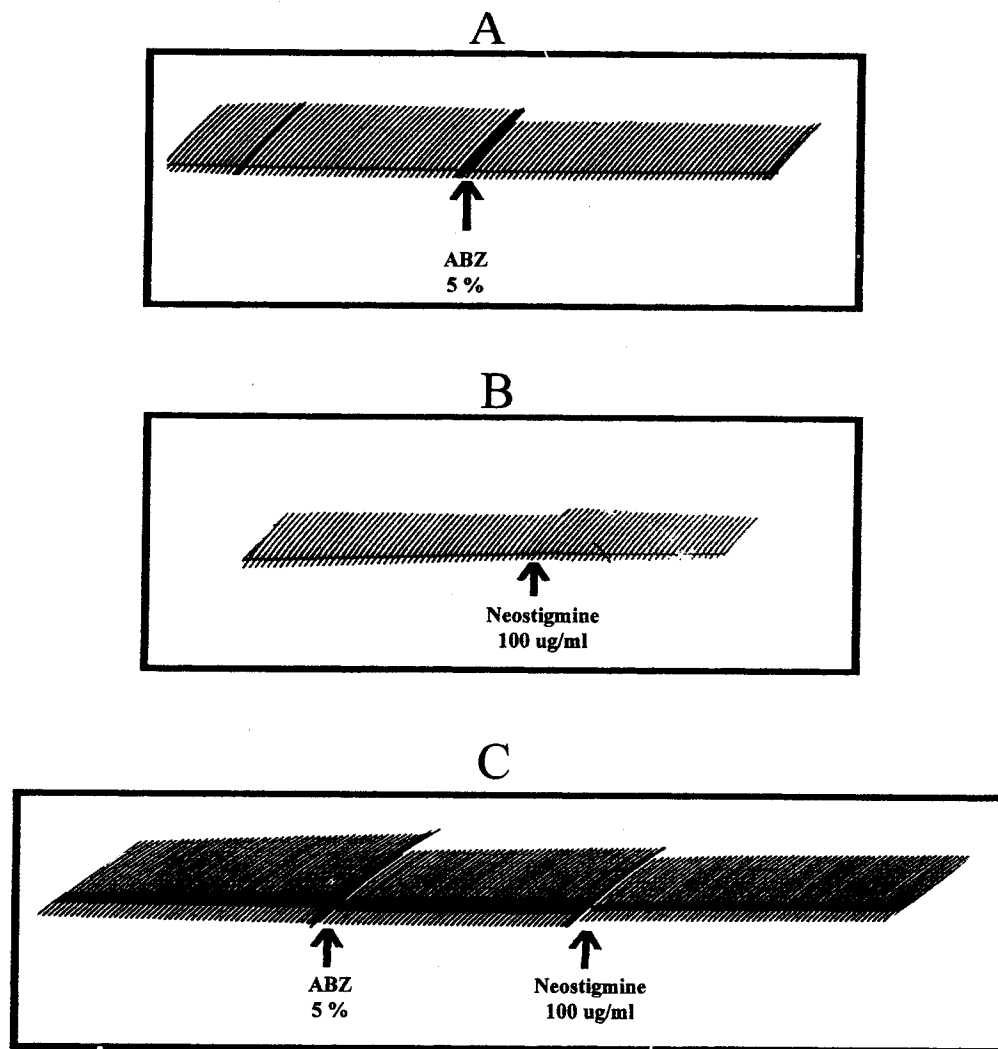


Plate (4): Representative trace for the effect of ABZ (5%) on the mechanical activity of the skeletal muscles. Gastrocnemius muscle preparation of the toad was mounted in Ringer solution at room temperature and the drug were perfused directly.

(A) Inhibitory effect of ABZ (5%).

(B) Effect of neostigmine (100 ug/ml) alone on the skeletal muscle.

(C) Notice that the anticholinesterase drug (neostigmine) did not block the depressor action of ABZ.

DISCUSSION

Recently, ABZ have been used in the treatment of hydatid cyst involving the heart (Simic *et al.* 1996; Ozdemir *et al.* 1997; Vicol *et al.* 1998). Although cardiac hydatidosis is uncommon, it may be revealed by cyst rupture and in such cases treatment requires surgery and associated medical management with Albendazole, which needs further evaluation (Brechignac *et al.* 1997; Suarez & Iannucci 1999). According to these new considerations, ECG was recorded during the first 24 hours after oral administration of ABZ (400 mg/kg). Although, the ECG is very useful for diagnosing and locating areas of cardiac disorders, the underlying electrical events and the resulting electrocardiographic changes are complex (Ganong 1997). In this investigation, the recorded heart rate shows a significant decrease after 12 & 18 hours from ABZ injection and nearly returned back to the control level after 24 hours. This negative chronotropic effect was concomitant with a non-significant prolongation in the P-R interval at the

same time points. The slowing heart rate and the temporary delay in the impulse conduction could be due to the postulated oxidative stress caused by ABZ-SO (Abd El-Rahman *et al.* 1999). This could induce a disturbance in the energy utilization in the heart and may contribute to cardiac dysfunction (Kaneko *et al.* 1993).

The current data revealed a gradual elevation in the R-wave amplitude with a significant difference only after 9 and 12 hours compared to the control values. This elevation reflects an increase in the myocardial contractility which could be a compensatory mechanism by which the heart trying to supply more oxygen to the hypoxic tissues.

On the other hand, the other ECG parameters, Q-T interval and T-wave amplitude, showed a mild non-significant changes during the time course. These finding were in agreement with Sir (1991) who reported that, some changes in the cardiovascular parameters were observed in dogs receiving 1 mg/kg Albendazole intravenously which were maximal at 30 min but returned to normal by 1 hour. Accordingly, it can be concluded that the main effect on the cardiac muscles might be induced by the oxidation reactions of the drug and its metabolite, however, it is mild and transient changes.

To confirm this postulation, we monitored the serum levels of CPK, which is present in high concentration in the myocardium, after administration of ABZ. CPK values started to increase significantly after 3 hours and reached its maximum level after 24 hours then started to decline to almost the control measures by the end of the time course. Damaged cells leak enzymes into circulation, and the rises in the serum levels of enzymes and isoenzyme produced by myocardial infarction play an important ancillary role in the diagnosis of this disease. The enzyme that most commonly measured in case of myocardial hypoxic damage is CPK since it is the most selective and sensitive test for myocardial infarction (Ganong 1997). It was reported that serum CPK increases about 6 hours after heart infarction and reaches a maximum after 18 hours (Thompson & Wootton 1970). It can be suggested that the elevation of the CPK values in the present study might be due to partial and transient abnormal leakage of this enzyme from the cardiac cells under the effect of the reactive metabolite of ABZ, Albendazole sulfoxide. It is well documented that ABZ is rapidly oxidized to ABZ-SO and then ABZ-SO₂ (Deliguoro *et al.* 1996) and these metabolites were detected in the heart in considerable concentrations over 48 hours of treatment with ABZ (Li *et al.* 1995). Oxidation reactions of drugs sometimes result in biotofication, which denatures protein and causes cellular damage (Muir 1980; Rang & Dale 1991).

More detailed investigations should be done on the pharmacodynamics of the drug on the cardiovascular system to confirm its safety. Also, it is important to emphasize that care should be taken in case of using Albendazole in the treatment of patients suffering from heart diseases.

Isolated perfused organ preparation offer several advantages over experimentation on intact animals, since it can give a definite evaluation of the role of exogenous chemicals on a particular organ or tissue (Mehendale 1984). Lawrenz *et al.* (1992) studied ABZ biotransformation in the gut by using an isolated perfused rat model. They reported that ABZ was biotransformed partly to ABZ-SO by the gut, where the metabolite but not the parent compound was absorbed. It is concluded that the gut has the capacity to biotransform Albendazole to only the first step, the sulphoxidation. Also, Lanusse *et al.* (1992) mentioned that the rate of ABZ oxidation into ABZ-SO is greater for cattle ruminal and ileal fluids than for sheep fluids under anaerobic

conditions *in vitro*. In the present work, the experiments performed on the isolated rabbit's duodenum revealed a stimulatory effect of ABZ. There was a dose-response relationship and the response plateaus at 5% ABZ concentration. Large dose of nicotine blocks the presser effects of ABZ on the isolated smooth muscles. On the other hand, atropine (muscrinic blocker) failed to prevent the stimulatory action of Albendazole. These results indicated that the effect of ABZ on the isolated smooth muscle of the gut is mediated through the parasympathetic ganglia. Also, it can be suggested that this stimulatory effect might be due to the oxidation reactions occurred during the partial biotransformation of the parent compound (ABZ) to its active metabolite (ABZ-SO) in the gut as documented by Lawrenz *et al.* (1992) and Lanusse *et al.* (1992).

Another *in vitro* study has been done in this investigation concerning the effect of ABZ on the neuromuscular junction of the gastrocnemius muscle of the toad. It was observed that ABZ decreased the mechanical activity of the muscle fibers. This inhibitory action could be related to a depolarizing blocking effect, since addition of neostigmine (anticholinesterase drug) to the medium failed to reverse the effect of the drug. It is well documented that anticholinesterase drugs enhance the cholinergic transmission at the neuromuscular junction and reverse the action of non-depolarizing neuromuscular blocking drugs (Rang & Dale 1991). Although the data indicated that ABZ has an inhibitory effect on the activity of the skeletal muscles, yet it still can be used as a chemotherapeutant for the treatment of parasitic infections in muscle tissues because the parent compound (ABZ) is rapidly metabolized and disappeared very quickly from blood (Li *et al.* 1995; Carpintero 1997; Garcia 1999).

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الملخص العربي

تقييم لتأثيرات الألبندازول (عقار مضاد للطفيليات) على النشاط الفسيولوجي للعضلات القلبية والملساء والهيكليّة لبعض حيوانات التجارب

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تهدف هذه الدراسة إلى متابعة وتقدير التغييرات التي تحدث في النشاط الكهربائي لعضلات القلب للفئران من خلال تسجيل رسم القلب الكهربائي (ECG) خلال الـ ٢٤ ساعة الأولى من حقن الألبندازول عن طريق الفم بجرعة علاجية واحدة (٤٠٠ مجم/كجم) وتحليل أجزائه المختلفة:

(Heart rate, P-R & Q-T intervals, R- & T- wave amplitudes)

وقد تم إجراء تجارب أخرى لتقييم تأثير هذا العقار على انقباض العضلات الملساء والهيكليّة المفصولة (*in vitro*) من الأرنب والصفدعة على التوالي. أوضحت النتائج حدوث نقص معنوي في معدل ضربات القلب بعد ١٢ ، ١٨ ساعة من المعالجة كما زادت قوة انقباض البطين

(R-wave amplitude) زيادة ذات دلالة إحصائية بعد ٩ ، ١٢ ساعة من إعطاء الألبندازول. وفي المقابل فإنه لم يطرأ أي تغيير معنوي على بقية المعايير الأخرى التي تم قياسها خلال فترة التجربة (٢٤ ساعة). ولمعرفة المزيد من التفاصيل عن تأثير هذا العقار على القلب تم تعيين مستويات أنشطة إنزيم الكرياتينين فوسفوكينيز في مصل الفئران المعالجة. وقد سجلت زيادة معنوية في نشاط هذا الإنزيم بعد ٣ ساعات ووصلت إلى أعلى قيمها بعد ٢٤ ساعة ثم عادت وانخفضت إلى قيم مقارنة لقيم المجموعة الضابطة بعد ١٩٢ ساعة. نستنتج من هذه النتائج أن هناك بعض التغييرات في النشاط الفسيولوجي للعضلات القلبية كنتيجة للتأثير المباشر للعقار ونواتج أيضية على الخلايا القلبية وأن هذه التأثيرات مؤقتة ومحددة.

أوضحت التجارب التي أجريت على العضلات الملساء لأمعاء الأرنب أن العقار يسبب زيادة في انقباض العضلات وأن هذا التأثير اختفى في وجود مادة النيكوتين في حين أن عقار الأتروبين لم يمنع حدوث التأثير المنبه للألبندازول. وبالنسبة لتأثير العقار على العضلة الساقية البطنية للضفدعة فإن غمرها بالألبندازول أضعف من قوة انقباضها وأن هذا التأثير استمر في وجود مادة النيوستجمين.

نستخلص من هذا البحث أنه يجب إجراء المزيد من الدراسات على هذا العقار وتأثيره على الجهاز الدوري للتأكد على سلامة استخدامه وبالأخص عند علاج المرضى الذين يعانون من أمراض قلبية.