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EFFECTS OF *PUNICA GRANATUM* SEED HYDROMETHANOL EXTRACT ON CONTRACTILITY OF ISOLATED AORTA IN FEMALE ALBINO RATS

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ABSTRACT:
The aim of the present study was to evaluate the physiological effect of the *Punica granatum* hydromethanol seeds extract on the contractility of isolated rat aortic rings. The isolated rat's thoracic aorta was placed in an organ bath containing Krebs solution and the contraction was recorded isometrically. The results demonstrated that *P. granatum* hydro- methanol extract (1.5 to 5 mg/ml) caused a significant relaxant effect on the contractions induced by phenylephrine (0.01 mM) with IC_{50} ± SEM of 2.682 ± 0.197 mg/ml and the percentage of relaxation for PE-induced contraction was 52.88 ± 0.831. In endothelium intact and denuded aortic rings, the extract induced more or less the same response, except at high concentrations used (4.5 – 5.0 mg/ml) in which the endothelium denuded rings produced a significant reduction in the percent of relaxation from 49.91 to 25.42. Relaxant effect of hydromethanol seed extracts on intact aorta was not affected by nitric oxide synthase sinhsibitor (L-NAME, $3*10^{-4}$), gaunyl cyclase inhibitor (methylene blue $1*10^{-5}$) and PGI_2 inhibitor (Indomethacin, $3*10^{-5}$), and thus, the percentages of relaxation were 59.85 ± 0.084, 58.59 ± 0.566 and 56.76 ± 0.693 respectively. In addition, incubation of aortic rings with the K+ channels blockers TEA, GLIB,, 4AP and $BaCl_2$, that Kca, KATP and Kv channels played no role on vasorelaxation induced by hydromethanol extract, while Kir enhanced the relaxation induced by the extract to76.40%. Finally, hydro methanol extract significantly enhanced dose-response relaxation after incubation of thoracic aortic rings with Nifedipine (10^{-6} M) to 91.91 % with IC_{50} ± SEM 1.774 ± 0.096. It can be concluded from the results of the current work that the fraction of *Punica granatum* hydromethanol seed extract has vasorelaxant effects on rat aortic which was partially dependent on endothelium, Kir and Ca channels.

KEYWORDS: Punica granatum, hydro methanol seeds extract, K+-channels blockers, Ca++-channels blocker, L-NAME, COX.

1. INTRODUCTION

Medicinal plants have been practiced for centuries as remedies for the handling of many human diseases because they carry a large number of bioactive components, most of them are of therapeutic values (Nostro *et al.*, 2000). Today, it is estimated that about 80% of people in developing countries still relies on traditional medicine based largely on species of plants for their primary health care. Herbal medicines are currently in demand due to their daily increased popularity (Dipak, 2012). The World Health Organization (WHO) has shown great interest in documenting the use of medicinal plants used by tribes from different regions of the world. Many developing countries have concentrated their efforts in documenting of the ethnomedical data on medicinal plants (Verma and Singh, 2008). Kurdistan, as other countries in the region, is rich in the flora, and many of them are used in folk medicine since long time ago (Shahbaz, 2010). In Kurdistan, in fact, the use of medicinal plants is described through history in the form of traditional medicines and oils that is the only medical treatment for people living in remote villages in the mountains (Amin *et al*., 2016).

In the archaic Ayurveda system of medicine, pomegranate has been extensively utilized as a source of traditional remedies for thousands of years (Woods and Woods, 2011). The seeds and juice are considered as tonic for the heart, throat, and eyes and used for different purposes, such as stopping nose bleeds and gum bleeds, toning skin, firming-up sagging breasts and treating hemorrhoids (Herlekar, 2014). Pomegranate, as a functional food has increased interested consumers due to the bioactive compounds present in the different parts of the plant (Viuda-Martos *et al*., 2011). The phenolic compounds that are distributed in different parts of the pomegranate plant contribute to the total antioxidant activity and may play a role in cancer prevention and therapy (Kim *et al.*, 2002). Some bioactive components reported in pomegranate arils in variable proportions are anthocyanins, ascorbic acid and β-carotene (Tzulker *et al*., 2007). Anthocyanins are responsible for the attractive color of pomegranate arils and some of the fruit's antioxidant activities (Borochov-Neori *et al*., 2009). Therefore it was worthwhile to investigate the role of calcium (Ca^{++}), potassium (K^{+}) channels subtypes', cyclooxygenase (COX) and denuded endothelium in the vascular relaxation induced by *P. granatum* hydro methanol vasoactive effect.

2. MATERIALS AND METHODS

2.1 Plant Materials

The fresh sour pomegranate fruits (*Punica granatum*), were collected from Armishte Agricultural field/Zakho during November 2014 were used during the current study. Pomegranates were washed and manually peeled; the seeds were carefully separated and washed with excess water for the removal of sugars and adhering materials. The seeds were dried in an oven at 40°C until constant weight, crushed in a grinder and sieved to obtain a fine powder.

2.2 Seed extraction

The extraction of P. granatum seeds fractions was performed in the advanced Physiology Research Lab / Department of Biology, Faculty of the Science, University of Zakho. The powder was

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extracted with 98 % hexane then 99 % ethyl acetate after that 99% methanol and finally with hydro- methanol, each for 48 hr. The extract was filtered with Whatman filter paper. The solvent of the filtrate was evaporated using rotary evaporator at 40°C temperature and the extracted powder was kept at -20oC until assay.

2.3 Preparation in electronic form

The extraction of *P. granatum* seeds fractions was performed in the advanced Physiology Research Lab / Department of Biology, Faculty of the Science, University of Zakho. The powder was extracted with 98 % hexane then 99 % ethyl acetate after that 99% methanol and finally with hydro-methanol, each for 48 *hr*. The extract was filtered with Whatman filter paper. The solvent of the filtrate was evaporated using rotary evaporator at 40°C temperature and the extracted powder was kept at -20^{o}*C* until assay.

2.4 Animals Breeding and Housing

Adult female albino rats (*Rattus norvegicus*) weighing 200-250 grams bred in the animal house of Department of Biology, Faculty of Science, University of Zakho, were used during the current study. Animals were housed under controlled environmental conditions at 20-24°C, relative humidity between 30–70%, and a photoperiod of 12 hours' light–dark cycle. The rats had free access to rodent food pellets (consist of 66.6% wheat, 25.6% soya, 4.4% oil, 1.5% limestone, 0.63% salt, 0.158% methionine, 0.062% choline chloride and 0.05% trace elements) (Shekha, 2010). The animals were supplied with dechlorinated tap water *ad libitum*. The animals were reared in rat cages (460 x 30 x 20 cm) bedded with shredded recycled wood ships at a density of 6 individuals/cages. The rats were reared under hygienic conditions with a daily cleanliness of the housing environment.

2.5 Aorta Preparation

The animals were injected intraperitoneally (IP) with heparin (1500 units/ kg body weight) and left for about 30 min to prevent blood coagulation and the possibility of damaging of the aorta endothelial layer (Fulton *et al*., 1996). Animals were then anesthetized with intraperitoneal injection of Ketamine (40 mg /kg) and Xylazine (10 mg/Kg). The descending thoracic aorta was rapidly removed and cleaned from extraneous connective and fatty tissues after transferring to a beaker containing an ice-cold Krebs solution aerated with carbogen (95 % oxygen (O_2) and 5 % Carbone dioxide (CO_2)]. Then, the isolated aorta cut into small rings approximately 2-4 mm long.

Isometric contractile responses were measured using the procedure described by Al-Habib and Shekha, (2010) with some modifications to study the vascular reactivity in the isolated aorta. Two stainless steel wires were carefully passed through the lumen of the aortic rings. One of them was anchored to the base of glass organ chamber and the other was connected to a force transducer (AD instrument Australia) which was coupled to the a trans bridge amplifier connected to Power Lab Data Acquisition System and a computer running chart software (Version 7) used for isometric tension measurement. Maximum care was taken during the assembly of aorta rings to avoid the damaging of the endothelium. The extents of contraction and relaxation were measured by the tension developed by the transducer and recorded by the system.

Prior to the experiment, the organ bath system set at 37°C was operated for at least two hours to allow the water in an organ bath to reach the thermal stability. After that, 10 ml of Krebs solution was placed inside the tissue glass chamber and continuously aerated with carbogen passed through the inlet at the base of the bath. Aortic rings were connected to the base of the chamber from one end and mounted to the transducer from the other end. Tissues were maintained under an initial tension of 2 g and allowed to equilibrate for 1 h during which bath solution was replaced every 15 min. The aortic segments were initially exposed to 10μM ($1X10^{-5}$ M) phenylephrine (PE) to test their functional integrity and 10μM ($1X10^{-5}$ M) acetylcholine (ACh) to test endothelium integrity. This was allowed by changing the bath medium several times until a stable resting tone was recorded, and then the experiments were started (Shekha, 2010).

After each experiment, bath solution was replaced every 15 min several times (3 to 4) with Krebs solution to allow the aortic rings to restore their initial tension. Then the relaxant effects of eight doses of *P. granatum* extracts (1.5 to 5 mg/ml) on the contractility of PE-precontracted aortic rings were studied.
In experiments carried on denuded aorta, endothelium was removed by gently rubbing the intimal surface the aorta with toothpick stick. The presence of functional endothelium was assessed in all preparations by determining the ability of acetylcholine (ACh, 10^{-5} M) to induce more than 50% relaxation in aortic rings precontracted with PE (10^{-5} M). Vessels were considered to be denuded of functional endothelium when there was no relaxation response to ACh (Nakamura *et al*., 2002).

2.6 Experimental protocols

In this study, cumulative dose-response relationships for the effects of *P. granatum* seeds hydromethanol extracts (1.5 to 5 mg/ml) aortic rings were measured. For all experiment, the vasorelaxant effects of *P. granatum* seed hydromethanol extracts were studied in aortic rings precontracted with PE ($1X10^{-5}$ M).

In the experiment for evaluating the role of endothelial cells, the denuded aortic rings were prepared as previously described; preincubated with L- NAME ($3X10^{-4}$ M), a nitric oxide synthesis inhibitor, methylene blue ($1X10^{-5}$ M) and indomethacin ($3X10^{-5}$ M) for 30 mins before PE pre-contraction. To evaluate the role of K^+ channels in vasorelaxation, the aortic rings were pre-incubated for 20 minutes with the following K^+ channel inhibitors, (TEA, 1 mM), (GLIB, $1X10^{-5}$ M), ($BaCl_2$, 1mM) and (4-AP, 1 mM). The blockers of K_{Ca} channel blocker, K_{ATP} channel blocker, K_{IR} channel blocker and K_V channel blocker respectively.Finally to clarify the functional role of Ca^{++} channel aortic rings with intact endothelium were incubated with nifedipine ($3X10^{-5}$), an L-type Ca^{2+} channel blocker for 20 min prior to contraction with PE.

2.7 Statistical Analysis

The statistical analysis was performed using two-way analysis of variance (ANOVA) supported by Bonferroni test when carrying out a pairwise comparison between the same dose of different groups using Graph pad prism program. Analysis of variance for repeated measurements was applied to data consisting of repeated observations at successive time points. P-values less than 0.05 ($P<0.05$) were considered as statistically significant. In all figures, the symbols (*, ** and ***) representing mean differences are significant at the 0.05, 0.01 and 0.001 levels respectively.

3. RESULTS AND DISCUSSION

3.1 Effect of hydromethanol seeds extract

A typical trace view from a representative experiment on relaxant effects of the hydromethanol extract on rat's PE-precontracted aorta is shown in Figure (1-A). A dose–response curve of the effect of hydromethanol extract against PE-induced contractions is shown in figure (1-B). Hydromethanol extract at concentrations from 1.5-3.0 mg/ml caused a non-significant relaxant effect in the PE (10^{-5}) precontracted rat thoracic aortic ring whereas at concentrations from 3.5-5.0 mg/ml produced a significant relaxant effect on precontracted thoracic rings.

Hydromethanol extracts produced a potent inhibitory effect on PE- induced contractions, with IC_{50} ± SEM of 2.682 ± 0.197 mg/ml (with an IC_{50} of CI 95% between 2.289 to 3.075). The percentage of relaxation for PE-induced contraction was enhanced 52.88 ± 0.831.

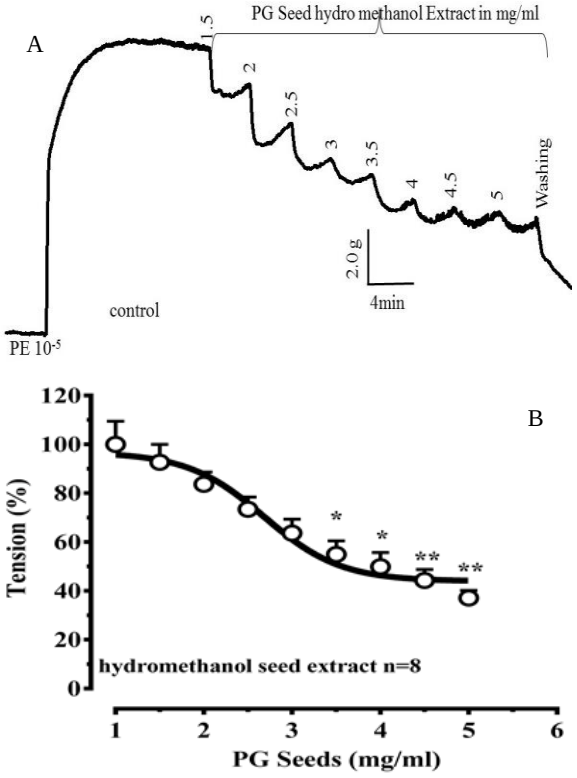

Figure 1. A typical chart view trace showing the vasorelaxant effects of different concentrations of *P. granatum* hydro methanol extract on rat aortic rings precontracted with 10^{-5} M PE (A). A cumulative dose-response curve for the effects of *P. granatum* hydro methanol extract on PE (10^{-5} M) induced contraction in rat's aorta (B).

Overall hydromethanol extract had a significant relaxation on aortic rings, this may be due to the presence of punicic acid and its congeners that are the most abundant compounds (80%) of the aqueous methanol extract that modulate NOS_2 and ultimately affect NO production (Costantini *et al*., 2014).

3.2 Role of Endothelium in Punica granatum Hydro Methanol seed extract on Induced Vasorelaxation in Rat Aorta

Lab chart traces from representative experiments and dose response curves on the relaxant effect of hydromethanol seed extracts on endothelium intact and denuded aortic rings are displayed in Figures (2). From the results, it is obvious that in endothelium intact aortic rings, cumulative addition of hydromethanol seeds extract (1.5 – 5.0 mg/ml), at the plateau phase of the PE (10^{-5}M) induced contraction caused a concentration - dependent inhibition in contraction of the aortic rings was observed. However hydromethanol extract at doses (1.5 – 4.0 mg/ml) induced a non-significant (P > 0.05) relaxation in denuded endothelium; whereas, at doses of 4.5 and 5.0 mg/ml, it produced significant inhibitory effects (P<0.05) and (P<0.01) respectively on the relaxation induced by hydromethanol extract. Thus, for endothelium intact and denuded aortic rings, the IC_{50} ± SEM 2.802 ± 0.209 mg/ml (with IC_{50} of CI 95% 2.386 to 3.219 mg/ml) and 2.225± 0.211 mg/ml (with IC_{50} of CI 95% 1.803 to 2.646 mg/ml) respectively. The percentages of relaxation for endothelium intact and denuded rings for hydro methanol extract were 49.91 ±0.418 % and 25.42 ±1.152%, respectively.

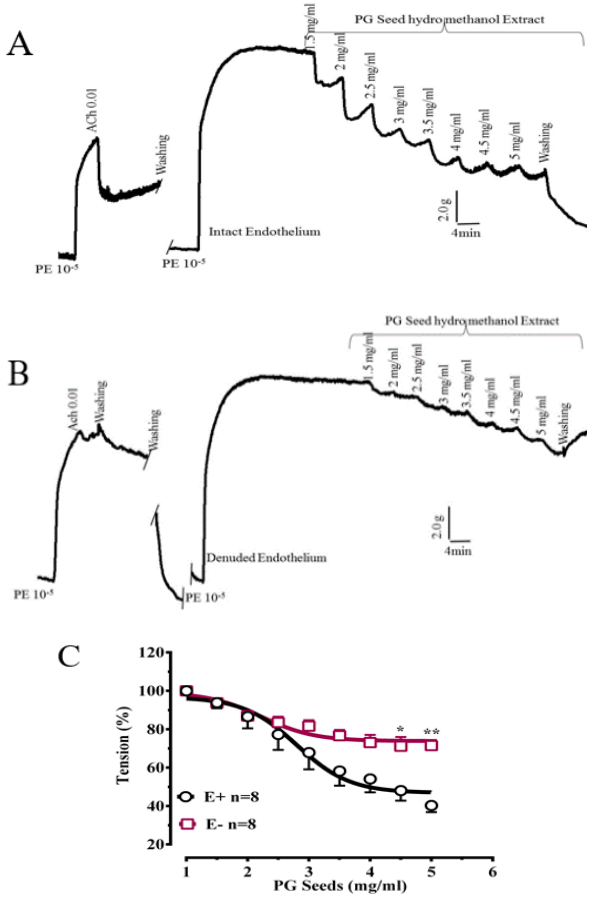

Figure 2. Typical chart view traces showing the vasorelaxant effects of different concentrations of *P. granatum* hydro- methanol extract on, endothelium-intact (A) and denuded (B) rat aortic rings. Cumulative dose-response curves for the vasorelaxant effects of hydromethanol extract on control and endothelium-denuded rat's aortic rings precontracted with 10^{-5} M PE (C).

These novel results indicate that the endothelium plays a partial role in the vasorelaxation induced by the hydro methanol extract. This was clearly indicated when treating the denuded aortic rings with hydromethanol extract, since the last two concentrations (4.5 and 5.0 mg/ml) caused a significant (P<0.05 and 0.01) attenuation in vasorelaxation. This implies that pomegranate causes vascular relaxation by two mechanisms: a direct effect on

the vascular smooth muscle that is independent of the endothelium and a mechanism that is dependent on the presence of a functional endothelium at high extract concentrations.

3.3 The Role of Endogenous NO, cGMP and PGI_2 on Vasorelaxant Action Induced by the Effect of Seeds Hydro methanol Extract in Rat's Aorta.

Cumulative dose-response curves (Figures 3, 4 and 5) display the effect of L-NAME, methylene blue and Indomethacin, on dose-response curves for the effect of hydromethanol against PE-induced contractions.
It is clear that the selected concentrations of L-NAME ($3X10^{-4}$), NOS inhibitor, Indomethacin ($3X10^{-5}$), PGI_2 inhibitor, and methylene blue ($1*10^{-5}$), a soluble guanylate cyclase inhibitor failed to affect the vasodilator responses to increase the concentrations of hydromethanol seed extract in PE-precontracted rat aortic rings. This clearly indicate that NO, PGI_2 and guanylate cyclase play no role in the vasodilation response to hydromethanol extract.

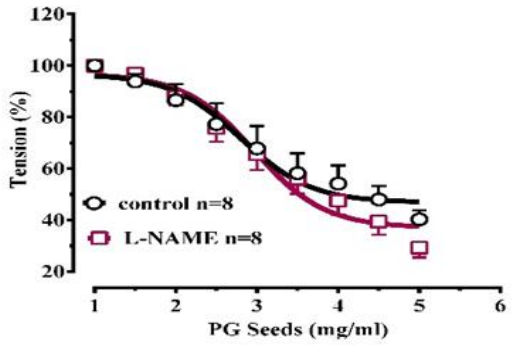

Figure 3. Cumulative dose-response curves for vasorelaxant effects of *P. granatum* hydromethanol extract on control and aortic rings preincubated with L-NAME ($3X10^{-4}$M), precontracted with 10^{-5} M PE.

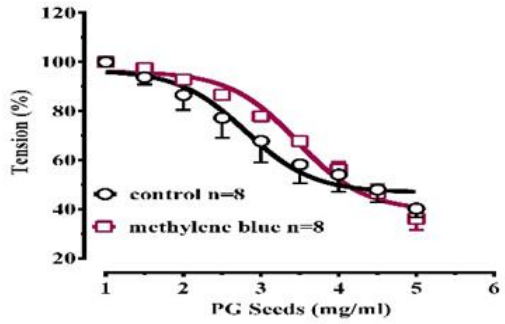

Figure 4. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydromethanol extract on control and aortic rings preincubated with methylene blue (3mM), precontracted with 10^{-5} M PE.

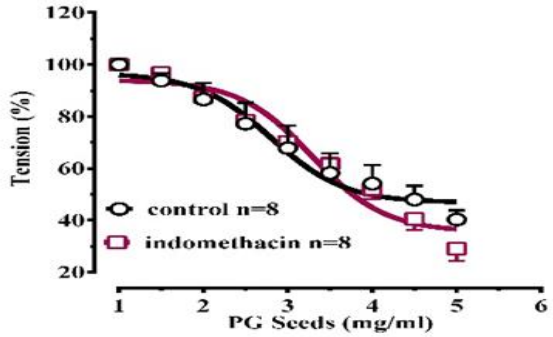

Figure 5. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydromethanol extract on control and aortic rings preincubated with Indomethacin ($3X10^{-5}$M), precontracted with 10^{-5} M PE.

3.4 The Role of Potassium Channels in Vasorelaxant Action Produced by P. granatum Seeds Extracts.

Aortic rings were preincubated for 20 minutes with the four types of K^+ channels blockers namely TEA, GLIB, $BaCl_2$ and 4-aminopyridine, individually, to find out their roles in vasodilator responses induced by hydro-methanol extract which discriminatory affected K_{Ca}, K_{ATP}, K_{IR} and K_V channels to a different extent. The dose response curves on relaxing effects of hydro methanol extract on rat thoracic aortic rings preincubated with above K^+ channel blockers, precontracted with PE that are shown in (Figures 6, 7, 8 and 9).

Pretreatment of the aortic ring with TEA, GLIB, and 4-aminopyridine, either did not modify the relaxation response as compared with control or mildly non-significantly enhanced the relaxant response. However, the effect of hydro methanol extract was significantly ($P<0.05$ - 0.01) enhanced in $BaCl_2$-treated aortic rings.

As the results indicate, the vasorelaxant effects of different concentrations of hydro methanol seeds extract were not affected to the same extent. At hydro methanol seeds extract concentration between 1.5-3.5 mg/ml, the vasorelaxant effect was not affected at all by the four K^+ channel blockers used. On the other hand, at concentrations of 4.0-5.0 mg/ml, the vasorelaxant response to hydro methanol seeds extracts was mildly enhanced and non-significantly in the presence of TEA and 4-AP, whereas in the presence of $BaCl_2$, the vasorelaxant response significantly enhances with IC_{50} ± SEM 2.819 ± 0.095 mg/ml (IC_{50} of CI 95% between 2.630 to 3.008 mg/ml), and the percentage of relaxation was enhanced to 76.4 ± 0.405%. However, at high hydromethanol extract concentrations (4.0-5.0 mg/ml), their relaxant response was not affected by the presence of GLIB.

These findings clearly suggest that K^+ channels may not play a role in the vasorelaxant effect of hydro- methanol extract in rat aortic rings, moreover, it is also reflecting some role of the K_{ir} which may be attributed to the inhibitory effects of the factors released from endothelium (Al-Habib *et al*., 2015). This implies that the vasorelaxant actions of hydromethanol extract against PE-induced contractions may involve inhibition of Ca^{+2} release from the sarcoplasmic reticulum stores and possibly other subtypes of K^+ channels.

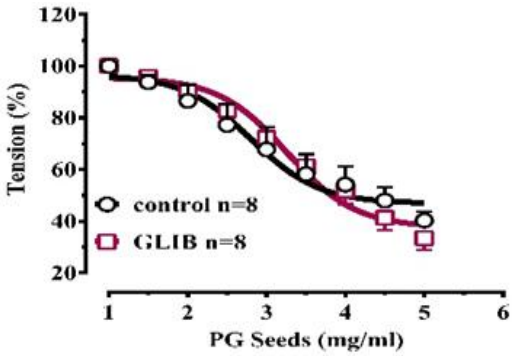

Figure 6. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydro methanol extraction control and preincubated aortic rings with GLIB (10^{-5}M), precontracted with 10^{-5} M PE.

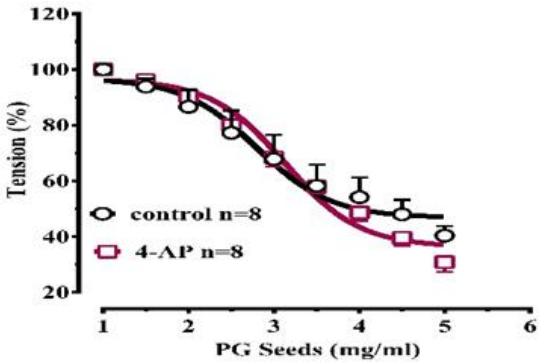

Figure 7. Cumulative dose-response curves for the vasorelaxant effects of *p. granatum* hydro methanol extract on control and preincubated aortic rings with 4-AP (1mm), precontracted with 10^{-5} M PE.

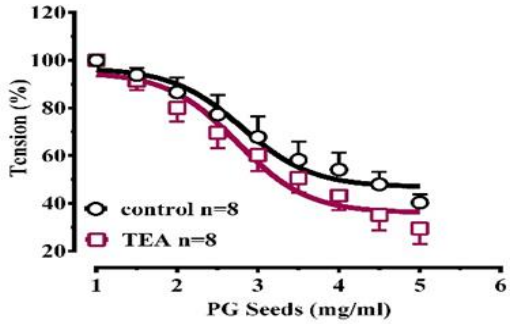

Figure 8. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydro methanol extract on control and preincubated aortic rings with TEA (1mM), precontracted with 10^{-5} M PE.

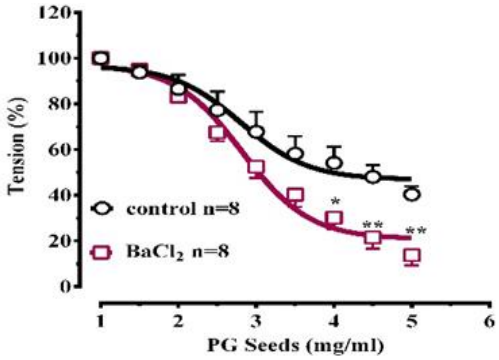

Figure 9. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydro methanol extract on control and preincubated aortic rings with $BaCl_2$ (1mM), precontracted with 10^{-5} M PE.

3.5 Investigation the mechanisms of the vasorelaxant action by involvement of calcium Channels.

Cumulative dose-response curves for the relaxant effect of hydro methanol seeds extract on aortic rings preincubated with Nifedipine, L-type calcium channel blocker and precontracted with PE are shown in figure (10).

In vasorelaxant effect on thoracic aortic rings preincubated with the Nifedipine 10^{-5} and precontracted with PE 10^{-5}, hydromethanol extracts vasorelaxant effect was enhanced at highly significant levels ($P<0.001$). This indicates that the role of *P. granatum* in the blocking of Ca^{+2} channel which indirectly participates and supports the vasorelaxation induced by *P. granatum*.

The IC_{50} ± SEM of control rings for hydro methanol extracts was 2.802 ± 0.2085mg/ml (IC_{50} of CI 95% between 2.386 to 3.219 mg/ml) whereas that of the treated rings was 1.774 ± 0.096 mg/ml (IC_{50} of CI 95% between 1.582 to 1.965), the percentages of relaxation was 91.91 ± 4.274 %, respectively.

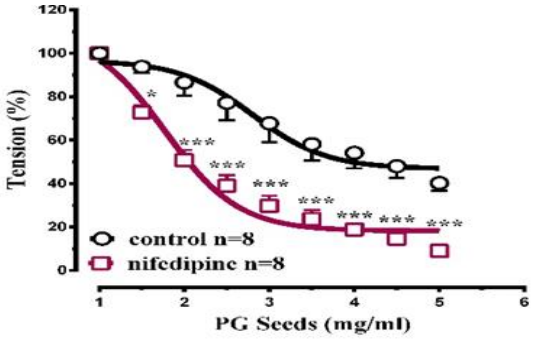

Figure 10. Cumulative dose-response curves for the vasorelaxant effects of *P. granatum* hydro methanol on control and preincubated aortic rings with Nifedipine ($3X10^{-5}$ M), precontracted with 10^{-5} M PE.

Ca^{+2}, which is essential for smooth muscle contraction, can be derived from the intracellular stores and/or extracellular fluid. Extracellular Ca^{+2} enters the cell via the voltage-gated dihydropyridine channels at the myocyte plasma membrane. Following the opening of this channel, Ca^{+2} enters down its concentration gradient. This will then trigger the release of more Ca^{+2} from the intracellular stores (Salleh and Ahmad, 2013).

Since most of the results of the current study are novel due to lack of information the comparison of the data is not possible at least at the moment. However, *P. granatum* is a rich source of a bioactive compound like phenolic and flavonoids (Anahita *et al*., 2015). Several mechanisms have been proposed to explain the vasorelaxant effects of the flavonoids including inhibition of contractile proteins such as protein kinase C, inhibition of enzymes such as cAMP-phosphodiesterase, and inhibition of Ca^{+2} release from intracellular stores (Ajay *et al*., 2003).

4. CONCOLUSION

The results of present research work indicate that fractions of *Punica granatum* hydromethanol seed extract has vasorelaxant effects on rat's aortic rings. Moreover, it induced endothelium-dependent and endothelium-independent vasorelaxation in aortic smooth muscle. Furthermore, it is shown that the effects are not mediated neither through NO, PGI_2, cGMP nor by potassium channels K_{ATP}, K_V and K_{Ca} channel. While there was an enhancement to the relaxation mediated by K_{IR} channel blocker. Finally the L-type Ca^{+2} channel blocker enhanced the relaxation caused by hydro methanol seed extract.

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کورتیا لێکولینێ:

ئەف ڤەکۆلینە ل سەر کارتێکرنا فسیولوژیا دەرهێنانا تۆقێ یا میپانولی ئاڤ ل سەر ڕهێن ماسۆلکێ شادەماران هاتیە کرن. راکرنا ڕهییێن شادەمارێن سینگی ژ جوردێن سپی و مەزن دێ کەینە د ئامیرێ (ORGAN BATH)، کو گێراوی کرێبس (KREBS SOLUTION) تێدابیت و کرژبوونا ماسۆلکان بشێوە یەکێ یەکسان وپێڤەرکری (ISOMETRICALLY) هاتیە تۆمارکرن. دئەنجامدا هاتیە دیارکرن، دەرهێنەرێ میپانولێ ئاڤێ ژ ڕێژا 1.5 هەتا 5 ملگم/ مل کارتێکرنەکا بهێز هەبوو بە IC50 ± SEM 2.682 ± 0.197 و هەروەسا ڕێژا سەدی یا خاڤبوون ژ کرژبوونێ ژ لایێ فینایلفرین ب ڕێژا 52.88 ± 0.831. هەروەسا ئەم دشێن دەربێخین، کو دەرهێنەرێ میپانولێ ئاڤێ کارتێکرنەکا بهێز هەیە ل سەر خاڤبوونا بۆرییێن خوینێ د بەراوردن دگەل دەرهێنەرییێن دی. بۆ هەلسەنگاندنا ڕۆلێ فاکتەرێن خاڤبوونا داتاشراوکری ژ تفکلێن اندوپیلیەمی ڕێگرێن جیاواز هاتینە بکار ئینان، وەکی **L**-نیترۆ ئەرجنین مەپیل ئەستر (L- NAME)، ئەندومیپاسین و METHYLENE BLUE. سەبارەت ئەوێن مە ل دەسپێکێ داینە دیارکرن، هەروەسا ئەف ڤەکۆلینە رولێ کەنالێن پوتاسیوم (**K**+) و کالسیوم ژ جورێن **L** بخوڤە دگریت. دەرهێنەرێ میپانولێ ئاڤێ کێمبوو ل IC50 ± SEM 0.211 ±2.225 ملگم/ مل و ڕێژا سەدی یا خاڤبوونێ برێژا 25.4 .±1.152% میپانولێ ئاڤی خاڤبوون ل سەر شادەماران ب (L-NAME 3*10-4) و (INDOMETHACIN 3*10-5) و (METHYLENE BLUE1*10-5) ل IC50 ± SEM2.966 ± 0.133و 3.286 ± 0.108 و 3.463 ± 0.08 ملگم/ مل و ڕێژا سەدی یا خاڤبوونێ ڕێژا 59.85 ± 0.084 و 58.59 ± 0.566 و 56.76 ± 0.693 لدویڤ ئێك یا هاتیە جێکرن. زێدە بەرسڤدانا خاڤبوونێ ژ ئەگەرێن میپانولێ ئاڤی هاتیە کرن.کو ب ئالوویرکرنا بازنێن شادماران بۆ ماوەیێ 20 خولەکان ب ڕێگرێن کەنالێن پۆتاسیوم (1 ملی مول GLIB 10-5)(TEA مولاری) و(1 ملی مول BACL2) و (AP1-4 ملی مول) ب IC50 ± SEM 2.744 ± 0.169 و 3.258 ± 0.1303 و2.819 ± 0.095 و3.128 ± 0.08 ڕێژا سەدی یا خاڤبوونێ ب ڕێژا 59.05 ± 0.799%و 3. 58.11 ± 0.58% و 76.4 ± 0.405% و60.22 ± 0.189% لدویڤ ئێك. پشتی ئالوویرکرنا بازنێن شادمارا سینگی بو ماوەی 20 خولەکان ب نیفیدیپین 10-6 مولاری . زێدەبوونەکا بەرچاڤ یا خاڤبوونێ ژ ئەگەرێن میپانولێ ئاڤی زێدەبوونەکا بەرچاڤ یا خاڤبوونێ ب IC50 ± SEM 1.774 ± 0.096 و ڕێژا سەدی یا خاڤبوونێ ب ڕێژا 91.91 ± 4.274% درست کر. و ژڤێرێ دیارە کو دەرهێنانەرێ تۆقێ یا میپانولی ئاڤ کارتێکرنەکا خاڤبوونێ هەیە ل سەر ڕهییێن شادەمارێن سینگی یێت جوردێن سپی.

خلاصة البحث:

تركزت الدراسة الحالية على تقييم التاثيرات الفسيولوجية لمستخلص البذورالمحضرمن الميثانول المائي (MeOH + H2O) على تقلص عضلة الشريان الابهر الملساء. ازيل الشريان الابهر الصدري من الجرذان البيضاء البالغة ووضع في جهاز (organ bath) الحاوي على محلول الكربس (Krebs solution) وسجلت التقلصات بشكل متساوو القياس (isometrically).اظهرت النتائج بان مستخلص الميثانول بتركيز (1,5-5 ملغ / مل) اظهر تقلصاً معنويا على التقلصات التي سببها فينيليفرين (PE) (0.01 ملم)، بEC50 ± SEM من 1.767 ± 0.231 ملغ / مل وبلغت نسبة التقلص للتقلصات الناتجة عن PE 89.22 ± 0.053. واظهر مستخلص الميثانول المائي بتركيز (1,5-5 ملغ / مل) استرخاناً معنوياً بIC50 ± SEM من 0.197 ± 2.682 ملغ / مل وكذلك النسبة المئوية لاسترخاء التقلص المحفزمن قبل PE كانت 0.831 ± 52.88. عند اضافة مستخلص الميثانول المائي عززت الاستجابة الاسترخائية لحلقات الأبهر المعاملة ب L - NAME (3 * 10-4)، اندوميثاسين (3 * 10-5)، والأزرق الميثيلين (1 * 10-5) بمقدار IC50 ± SEM2،966 0.133 ±، 3.286 0.108 ± و3.463 ± 0.082 على التوالي. وبلغت النسبة المئوية للاسترخاء 59.85 ± 0.084، 58.59 ± 0.566 و56.76 ± 0.693 على التوالي. و ايضا حصلت زيادة في استجابة الاسترخاء المعامل بالميثانول المائي، عند الحضن بالحاصرات القنوات البوتاسيوم ، TEA (MM1)، GLIB (5-10)، BaCl 2 (1MM) وAP (1MM) -4. بمقدار IC50 ± SEM2.744 ± 0.169، 3.258 0.1303 ±، 2.819 0.095 ± و3.128 ± 0.08. وبلغت النسبة المئوية للاسترخاء 59.05 ± 0.799%، 3. 58.11 ± 0.58%، 76.4 ± 0.405% و 60.22 ± 0.189% على التوالي. بعد حضن حلقات الشريان الابهر الصدري ب نيفيديبين (10-6 م) لمدة 20 دقيقة، حصلت زيادة ملحوظة في اثباط التقلصات التي سببها فينايلفرين PE عند معاملتها بالميثانول المائي أيضا سبب زيادة ملحوظة في الاسترخاء بمقدار IC50 ± SEM1.774 ± 0.096 وبلغت نسبة الاسترخاء 91.91 ± 4.274%. لذلك فإن النتائج تشير إلى أن مستخلص البذورالمحضرمن الميثانول المائي له آثار استرخائية على حلقات الصدري للفئران.