

CARDIOVASCULAR EVALUATION OF *RUELLIA PATULA* AND *RUELLIA* *BRITTONIANA*

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SUMMARY : Cardiovascular profile of *Ruellia patula* and *Ruellia Brittoniana* was carried on isolated rabbit heart. Crude extract, butanolic and aqueous layer of both plants were tested on heart rate, force of contraction and coronary flow. Digoxin was used as a controlled drug. All the fractions showed an increase in force of contraction except n-butanolic fraction of *R. brittoniana* which exhibited depression in all parameters. Coronary flow and heart rate displayed non significant decrease. Therefore it was concluded that the given *Ruellia* plants are of cardiostimulant nature.

Key Words: *Ruellia patula*, *R. brittoniana*

INTRODUCTION

Ruellia species (Acanthaceae) is distributed in tropical and temperate regions of both hemispheres, whereas in Pakistan it is found in wild state in the provinces of Baluchistan and Sindh. *Ruellia patula* Jacq. is widely distributed in Africa, Arabia and South West India, while *R. brittoniana* E. Leonard is a native of Mexico and grows as an ornamental. Both species abundantly grow in Pakistan, and found in Karachi as erect spreadly perennial shrubs (6, 7). *Ruellia* species have been utilized in folkloric medicine to cure eye sore, gonorrhoea, syphilis, and renal infections (3, 9). *R. prostrata* is given as a remedy for gonorrhoea. Roots of *R. suffruticosa* are used in gonorrhoea, syphilis, renal infections and to cause abortion. *R. repens* is used as a remedy for cough wounds, scalds, toothache and stomachache in China. In Indonesia fresh and dried leaves of *R. napefera* are used in the treatment of kidney stones (10).

From the whole plant of *Ruellia patula* two lignan glycosides 5,5-dimethoxy-1- β -D-glucopyranoside and lyoniresinol-9- β -D-glucopyranoside (8) and *R. brittoniana*, 2- β -D-galactopyranosyl glycerol hexaacetate (1) were isolated and reported.

No pharmacological evaluation on cardiovascular system has been reported prior to this report, which is a preliminary investigation on isolated heart specially on three parameters, i.e. force of contraction, heart rate and

coronary flow. Though cardiovascular evaluation has already been carried out on two fractions of *R. patula* previously (8). A comparative account of the results on cardiovascular profiles of two species i.e. *R. patula*, *R. brittoniana* and digoxin on isolated heart is now being reported in this communication.

MATERIALS AND METHODS

Extraction and isolation

The extraction and isolation of these two species has been reported previously (1, 8)

The plants of *Ruellia patula* and *R. brittoniana* were collected from the Karachi University Campus in September 1987. The plants were identified by Prof. Dr. S. I. Ali and Mr. Abdul Ghafoor, Department of Botany, University of Karachi and a specimen was deposited in the department herbarium.

The whole plant (12 kg) was chopped into small pieces, and was percolated in MeOH. The extract so obtained was concentrated under reduced pressure which gave a dark colored residue and to it water was added. The insoluble material was removed by filtration through celite. The filtrate was taken up in petroleum ether, and the organic soluble part was discarded. The aqueous phase was fractionated first with EtOAc and later with saturated n-BuOH Aqueous fraction was thereafter lyophilized.

Pharmacological screening

In this study isolated perfused rabbit heart method as described by Langendorff with modifications was employed. Briefly healthy (1-2 Kg) of either sex were used. A blow on the neck of the rabbit made them unconscious. The chest was opened and the heart was carefully removed in petridish filled

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with McEwen's solution (NaCl: 7.60 g/l, KCl: 0.42 g/l, CaCl: 0.24 g/l, NaHCO₃ 2.10 g/l, glucose: 2.00 g/l, sucrose 4.50 g/l), and bubbled with oxygen. Isolated heart was mounted on the apparatus with the help of glass cannula and perfused with McEwen's solution at 37°C. Recordings were made by the help of isotonic transducer (Harvard) on chart recorder (Eyela). Parameter measured were 1) force of contraction (height in mm), 2) heart rate (beats/min), 3) coronary flow (ml/min). Atmospheric pressure on the heart was kept at 45 mmHg approximately. No changes were introduced during these experiments.

Dose regimen

The extracts and their fractions with doses which gave the maximum contractile force in this study were as follows.

1. *R. patula* crude extract 1 mg to 16 mg
2. *R. brittoniana* crude extract 1 mg to 16 mg
3. *R. patula* aqueous layer 1 mg to 32 mg
4. *R. brittoniana* aqueous layer 1 mg to 16 mg
5. *R. patula* n-butanol layer 1 mg to 64 mg
6. *R. brittoniana* n-butanol layer 1 mg to 64 mg
7. Digoxin standard drug 1 µg to 40 µg

Plant extracts were freeze dried and doses were prepared from the powdered form by dissolving 100 mg/10 ml in physiological solution (10 mg/ml). This concentration was used as a stock solution and further dilutions were made from this stock solution. Digoxin was prepared accordingly, and 1 mg/ml stock solution was used for further dilutions.

RESULTS

All crude extracts and fractions of these two plant spp. along with digoxin were subjected to test their activity on three parameters of the isolated rabbit heart i.e. a) force of contraction, b) heart rate, c) coronary flow. The changes in these parameters were shown as % change from control values.

Crude extracts

i) *R. patula*: (Figure 1) showed the effect of crude extract of *R. patula* for all three parameters. The maximum contractile force increase i.e. 20% was shown by 8

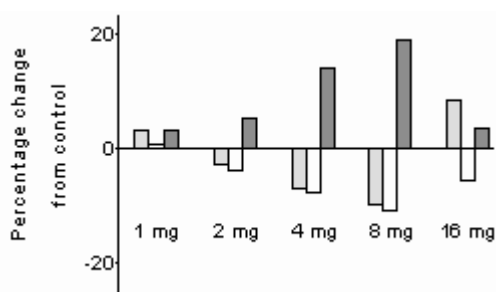


Figure 1: Showing the effect of crude extract of *R. patula* on cardiac parameter of isolated rabbit heart.

mg dose. Heart showed non-significantly negative chronotropic effect. The same negative effects were also observed on coronary flow with all doses expect the first dose.

ii) *R. brittoniana*: The maximum positive inotropic effect by this extract was also established (+36%) at 8 mg which was better than *R. patula*. Slight increase in heart rate and coronary flow at initial doses were ascertained as well (Figure 2).

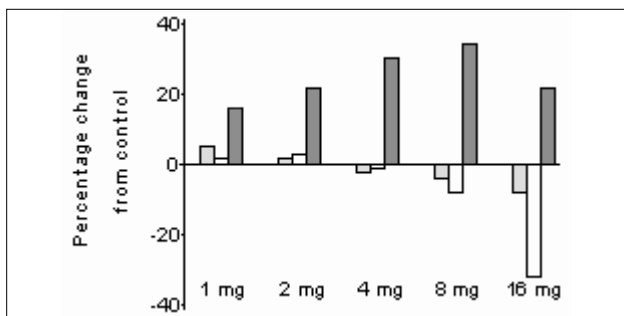


Figure 2: Showing the effect of crude extract of *R. brittoniana* on cardiac parameter of isolated rabbit heart.

Aqueous fraction

i) *R. patula*: Changes by this fraction has been shown in Figure 3. A positive inotropic effect by all doses (maximum 48% up to 16 mg) was complied with biphasic response on heart rate. The decrease of 20% in heart rate was seen. Coronary flow showed a constant decrease at all doses which was about 40%, an unusual effect. Increase in contractile force was dose dependent.

ii) *R. brittoniana*: (Figure 4) showing the effect of aqueous fraction of *R. brittoniana*. Contractile force increased dose dependently and maximum increase was up to 28% at 8 mg. Heart rate and coronary flow also exhibited a decrease dose dependently expect that 1 mg coronary flow was increased.

n-butanolic fraction

i) *R. patula*: A dose dependent positive inotropic effect was found by this fraction of *R. patula* (Figure 5). A decrease in two other parameters i.e. in heart rate and coronary flow was also recognized.

ii) *R. brittoniana*: (Figure 6) Surprisingly this fraction showed complete negative effect on all the parameters which categorize this as a cardiac depressant. Maximum depression was set forth in coronary flow i.e. 50% at 64 mg. Heart rate conducted a 42% decrease while 20% decrease in contractile force was displayed at the same 64 mg.

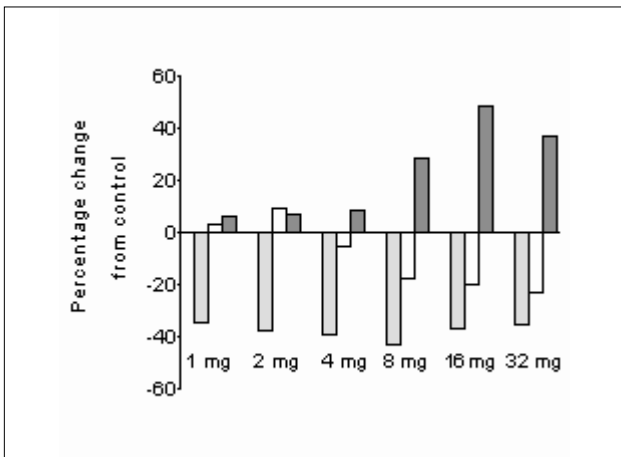


Figure 3: Showing the effect of aqueous layer of *R. brittoniana* on cardiac parameters of isolated rabbit heart.

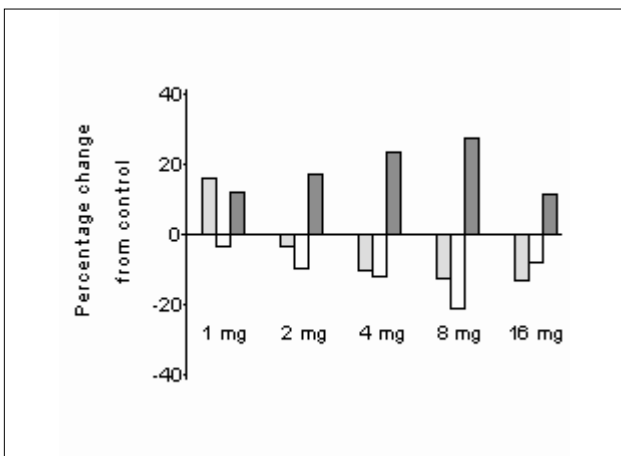


Figure 4: Showing the effect of aqueous layer of *R. brittoniana* on cardiac parameters of isolated rabbit heart.

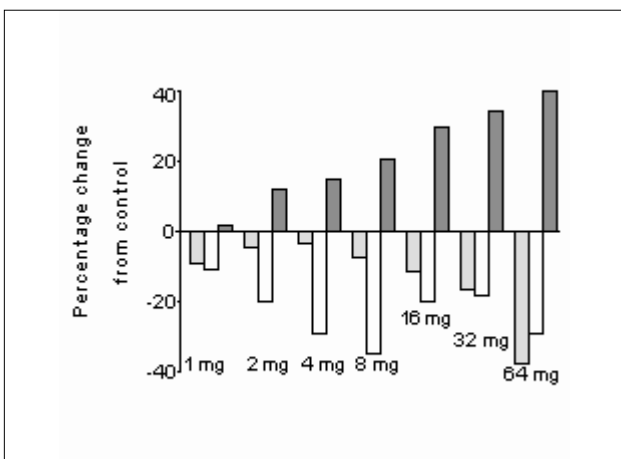


Figure 5: Showing the effect of n-butanolic layer of *R. patula* on cardiac parameters of isolated rabbit heart.

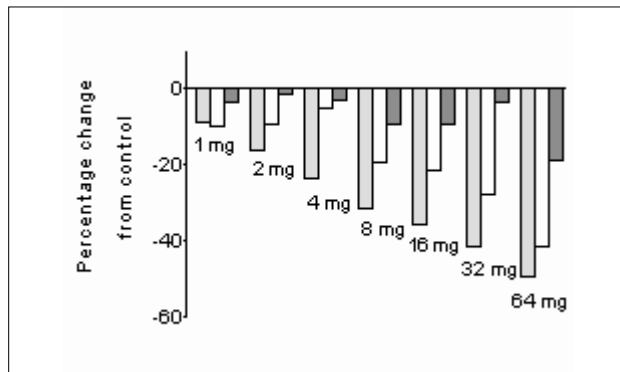


Figure 6: Showing the effect of n-butanolic layer of *R. brittoniana* on cardiac parameters of isolated rabbit heart.

Digoxin

This drug has been used as a standard cardiotoxic agent to compare the effect with plant extracts. This drug manifested a dose dependent increase in contractile force. A dose dependent decrease in coronary flow and a non-significant decrease in heart rate was also noticed (Figure 7).

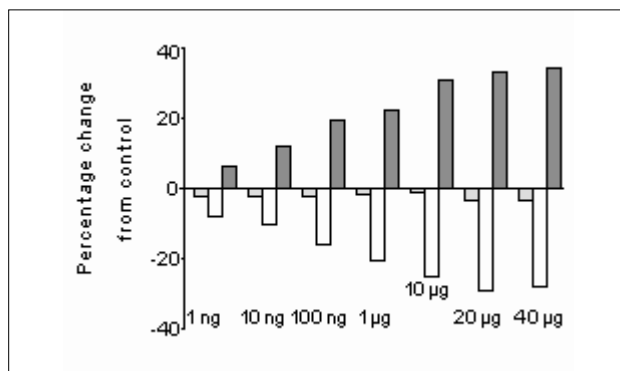


Figure 7: Showing the effect of Lanoxin on cardiac parameters of isolated rabbit heart.

DISCUSSION

During the pharmacological screening of various plant extract for their cardiovascular properties in this laboratory (11,12), it was revealed that very few plant extracts possessed a good cardiotoxic properties. It was decided to evaluate this property of these compounds initially on isolated rabbit heart. Two plants were selected which showed good activity as a cardiotoxic i.e. *Ruellia patula* and *R. brittoniana*. The effect of crude extract, n-butanol and aqueous fractions of these two plants on cardiovascular profile is being reported for the first time. A comparison among these fractions as well as with digoxin was also made.

The chemical nature of both plant spp. extract - revealed the presence of new lignan glycosides (1, 8), whereas digitalis contains steroidal cardioactive glycoside hold a unique position as a therapeutic agents by virtue of their specific and powerful actions on the heart.

These steroidal cardiac glycosides are mainly obtained from *Digitalis*, *Strophanthus*, *Acokanthera*, *Urginea*, *Apocynum*, *Convallaria* (14) and other plants which elaborates steroidal glycosides. Cardiotonic drugs are not replaced yet by other adequate substitutes. This study may lead the efforts in this directions for new substitutes.

In the present study crude extract of *R. brittoniana* present to view a better cardiotonic effect than *R. patula*. It is ostensible that up to 8 mg dose both extracts showed significant responses as cardiotonic i.e. increase in contractile force and a non significant decrease in heart rate and coronary flow. These effects appears to be in accordance with the digoxin results. It is evident from the results that responses produced by the crude extract of *R. brittoniana* has a better compatibility with digoxin in contractile force while both crude extracts caused a 8% decreased in coronary flow. Digoxin indicated a 35% decrease with no significant change in heart rate which suggest a better effect on coronary flow by these two extracts. However the crude extract of *R. brittoniana* should further be evaluated by other techniques in intact animals before establishing it as a cardiotonic.

The effects of Digitalis and steroidal cardiac glycosides in normal individual argument the strength and speed of myocardial contraction (13).

In congestive heart failure the increased contractile force by Digitalis produce increased cardiac output, decreased heart size, venous pressure and blood volume (5). Decreased heart rate may be due to a) vagal action b) by extra vagal action i.e. direct depression action on A-V conduction system (2), and all this is due to small doses. The large doses of digoxin and cardiac glycosides increase the excitability (2), and may produce dysrhythmias. Cardiac slowing is not a significant feature of Digitalis action in normal man (4). Digitalis by improving the cardiac output will reduce the heart rate. The change in rate is secondary to the improvement of the circulation and not the primary therapeutic action of the drug (5).

Coronary circulation is not directly affected by Digitalis, but an improvement in coronary flow occurs secondary to the improvement in cardiac output and slowing of the heart (13).

In present study the extracts and their fractions decreased the coronary flow and heart rate. The reduction in heart rate may be explained on the assumption of above discussion but a significant decrease in coronary flow by some fractions, and even by digoxin may need further evaluation. Perhaps this activity may be explained on the basis that these fractions and digoxin were tested on a) isolated rabbit heart with no or little compensatory mechanism, b) the reported activity of digoxin are mainly an congestive heart failure with reduced cardiac output.

Cardiac depression shown by n-butanolic layer of *R. brittoniana* are not illustrative expect that this fraction may have completely devoid of the glycosides which were found in other fractions during the separation process.

It is difficult to test these extracts on human like conditions but further studies under experimental conditions may reveal several interesting results of these compounds. More experimental work is required before justifying the activities of these agents as that of cardiac glycoside.

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