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Original Article

Cardiotonic Activity of Aqueous and Alcoholic Extracts of *Leea macrophylla*

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ABSTRACT

Present study was carried to evaluate the cardiotonic effect of aqueous and alcoholic extract of Leea macrophylla. This was studied by isolated frog heart perfusion technique. Calcium free ringer solution was used as vehicle for administration of Leea macrophylla extracts and standard drug Digoxin. Both the extracts of plant Leea macrophylla show increase in heart rate and force of contraction in normal heart. The current study reveals that Leea macrophylla improves the function of a hypodynamic heart which is indicative of its cardiotonic activity.

Key words: Leea macrophylla; isolated frog heart perfusion technique; cardiotonic effect.

1. INTRODUCTION

Leea macrophylla (Roxb.) (Family: Leeaceae) is a herb or herbaceous shrub with a very big size leaf like an elephant-ear. The plant parts of *Leea macrophylla* are used by tribal people in cold, cough, headache, tetanus etc. [1-2] It has also Ethnobotanical uses in goiter, gastric tumor, lipoma body pain and rheumatic pain. [2-4] Though the plant has traditionally been used in the treatment of various types of diseases, to the best of our knowledge, there have been no scientific reports on the cardiovascular system effects of this plant.

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2. MATERIALS AND METHODS

Experimental Animals:

Frogs of *Rana tigrina* species from the animal house froggery of Govt. College of Pharmacy Karad were used for the study and were maintained as per CPCSEA guidelines. A prior approval was obtained from the Animal Ethics Committee of GCOP, Karad.

Instruments used: Sherington Rotating Drum for tracing and recording resposes, Sterling's heart lever and Symes venous cannulae.

Drug: The marketed Digoxin (Sun Pharma Ltd.) was obtained from the local market.

Preparation of Extracts:

The plant species *Leea macrophylla* [Roxb.ex Hornem] belonging to Family: Leeaceae was collected from Kalgaon village Taluka. Patan, District- Satara and authenticated at Botanical department of Yashwantrao Chavan college of science, Karad. The plant was dried under sunlight and fine powder of the plant was prepared by using hand grinder.

Preparation of Aqueous Extract: powder was mixed with 30ml distilled water boiled for 30 minutes in round bottom flask attach with reflux condenser. The material was filtered whatman filter paper no 40 and filtrate was collected.

Preparation of Alcoholic Extract: powder was mixed with 30 ml alcohol and 10 ml distilled water boiled for 30 minutes in round bottom flask attach with reflux condenser. The material was filtered whatman filter paper no 40 and filtrate was collected. Filtrate was collected in porcelain dish. Alcohol was evaporated and then adds 4ml distilled water.

Preparation of digoxin solution:

Various different concentrations were made with distilled water. The prepared samples were evaluated for their cardiotonic activity and were treated as reference standard.

Evaluation of cardiovascular effects: [5-8]

Isolated frog heart perfusion model was used to evaluate the activity of various concentrations of *Leea macrophylla* extracts. The frog was pithed and pinned to the frog board. A midline incision was given on the abdomen, the pectoral girdle was removed and the heart was exposed. The pericardium was carefully removed and few drops of frog ringer were poured over the exposed heart. The inferior vena cava was traced, a thread was tied around it and a small cut was given in order to insert the venous cannula. The cannula was inserted in the vein and the thread was tied to assure that the cannula was in place which was in turn was connected to a saline bottle containing frog ringer solution. A small cut was given to the aorta for the ringer to come out. Heart was isolated and attached to the stand with moderate flow of ringer. A thin pin hook was passed through the tip of the ventricle and with the help of a fine thread attached to the hook; it was tied to the free limb of the Sterling's heart lever which was fixed to a stand. A proper tension was adjusted by altering the height of the lever. The normal heart rate was noted. All test samples were administered in different doses viz. 0.1ml, 0.2ml, 0.4ml. The rate and force of heart contraction were noted.

Evaluation of cardiotonic activity: [5-8]

Above model was used to evaluate the cardiotonic activity of various concentrations of *Leea macrophylla* extracts. Except, for this experiment was carried out by using Ca++ free ringer solution/modified ringer (Hypodynamic ringer solution) instead of frog ringer solution was used. Composition of hypodynamic frog ringer solution is as follows- Sodium chloride- 6.5 gm, Potassium chloride - 0.14 gm, Calcium Chloride- 0.03 gm, Sodium bicarbonate -0.2 gm, Glucose- 2 gm and Distilled Water up to 1000 ml.

The basal cardiac contraction was recorded on a kymograph after the administration of calcium free ringer solution. The average basal heart rate and the contraction amplitude were noted as beats/min and in mm respectively. The responses of digoxin and *Leea macrophylla* extract at various concentrations were recorded on kymograph and their cardiac activity in terms of heart rate and height of force of contraction was noted and compared. The frog heart was washed with ringer solution after every administration of test extract and reference drug till it was brought to normal state.

Statistical analysis:

Results are presented as means + SEM (standard error of mean), except the Cardiac outputs that are presented as geometric means. Statistical significance between groups was calculated by means of analysis of variance followed by students T- test, $P < 0.05$ was considered significant.

3. RESULTS

Effect of *Leea macrophylla* extracts on normal isolated frog heart preparation

The present results shows that the *Leea macrophylla* extracts has significant effect observed on the height of force of contraction (positive inotropic effect) or the heart rate (positive chronotropic effect) when the dose of *Leea macrophylla* extracts was increased. The details of the observed effects are summarized in Table-1 and depicted in Figure-1.

Effect of *Leea macrophylla* extracts on hypodynamic isolated frog heart preparation

Calcium free Ringer solution was used as vehicle for administration of *Leea macrophylla* extracts as a test extract and digoxin as a standard. The present results indicated that a significant increase in height of force of contraction (positive inotropic effect) and in heart rate (positive chronotropic effect) at a very low concentration (50 µg/ml) was observed with *Leea macrophylla* extracts as compared to the same dose of a standard digoxin. The details of the observed cardiotonic effects are summarized in Table-2 and depicted in Figure-2.

These preliminary studies confirm the better cardiotonic activity of *Leea macrophylla* extracts. All the concentrations of *Leea macrophylla* extracts restore the cardiac activity of Hypodynamic frog heart i.e. it increases

rapidity and force of contraction. It was found that higher concentration of *Leea macrophylla* extracts showed better response as compared to the lower ones. It is interesting to know that *Leea macrophylla* extracts has rapid onset of action compared to Digoxin.

Table 1: Effect of different concentrations of *Leea macrophylla* extracts on normal heart of frog

Drug	Dose in ml	Concentration at different doses (µg/ml)	Heart rate [HR]	Height of force of contraction [HFC]	Cardiac output CO= HR X HFC
Aqueous Extract	Normal	0	36.33 ± 0.33	14.66 ± 0.33	532.59
	0.1 ml	50	37.66 ± 0.11	14.98 ± 0.57	564.14
	0.2 ml	100	39.33± 0.22	15.13 ± 0.0	595.06
	0.4 ml	200	41.61 ± 0.44	15.66 ± 0.33	651.61
Alcoholic Extract	Normal	0	36.33 ± 0.33	15.12 ± 0.34	549.30
	0.1 ml	50	38.33 ± 0.11	18.33 ± 0.33	702.58
	0.2 ml	100	40.33 ± 0.11	17.66 ± 0.33	712.22
	0.4 ml	200	42.23 ± 0.24	17.85 ± 0.57	753.80

Table 2: Effect of different concentrations of Digoxin and *Leea macrophylla* extracts on hypodynamic heart of frog

Drug	Dose in ml	Conc. at different doses (µg/ml)	Heart rate [HR]	Height of force of contraction [HFC]	Cardiac output CO= HR X HFC
DIGOXIN	0.1 ml	50	37.25 ± 0.85	16.25 ± 0.62	605.31
	0.2 ml	100	39.0 ± 0.70	18.75 ± 0.25	731.25
	0.4 ml	200	41.0 ± 0.70	22.12 ± 0.70	906.92
Aqueous Extract	0.1 ml	50	36.33 ± 0.44	16.25 ± 0.48	590.36
	0.2 ml	100	38.23 ± 0.55	17.25 ± 0.47	659.46
	0.4 ml	200	40.14 ± 0.77	18.50 ± 0.64	742.59
Alcoholic Extract	0.1 ml	50	37.23 ± 0.25	17.02 ± 0.32	633.65
	0.2 ml	100	39.33± 0.51	17.87 ± 0.22	702.82
	0.4 ml	200	41.21 ± 0.54	18.89 ± 0.77	778.45

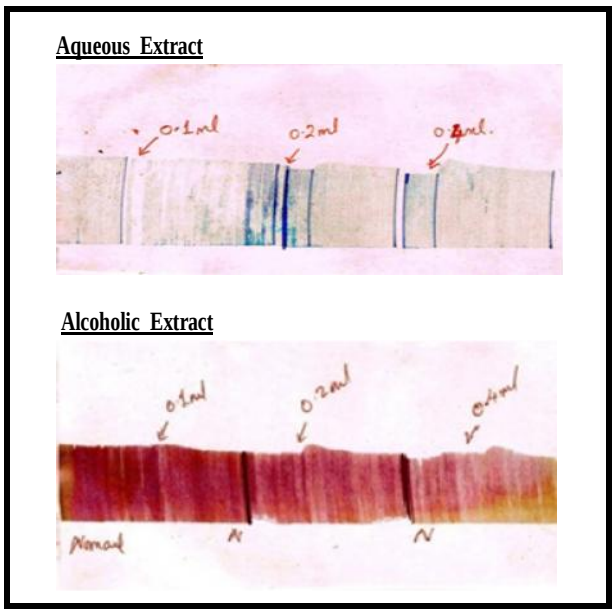

Fig 1: Kymographs showing effect of the *Leea macrophylla* on normal frog heart

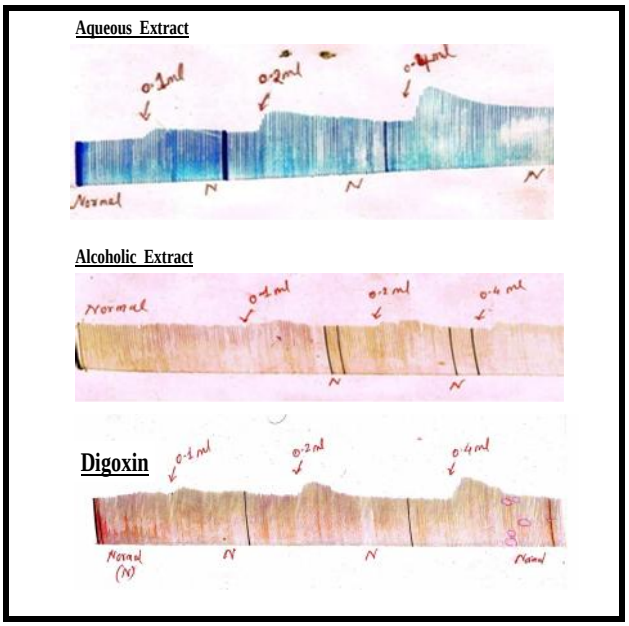

Fig 2: Kymographs showing effect of the *Leea macrophylla* extracts on hypodynamic frog heart

4. DISCUSSION

Cardiovascular effects (Cardiotonic activity) of *Leea macrophylla* extarcts

The effects of the extracts of *Leea macrophylla* on cardiovascular system using their different concentrations & comparison of its cardiotonic activity with digoxin have not been previously reported.

From the observation of the current study the extracts of *Leea macrophylla* was found to restore cardiac activity of the hypo dynamic frog heart, which was characterized by positive ionotropic and chronotropic action on the myocardial muscles of the perfused frog heart.

Different classes of phyto compounds of medicinal importance have been detected in *Leea macrophylla* extracts including alkaloids, flavonoids, tannins, triterpenes and sterols. It has been previously reported that flavonoids and phenolic compounds are potent antioxidants and are believed to prevent cardiovascular diseases and exhibit a wide range of cardiovascular effects [9].

The cardiotonic activity exhibited has positive ionotropic and chronotropic effect on isolated frog's heart which may probably be due to the presence of flavanoids. The present study promises a lot of scope for further research on its cardiac activity. Thus, in future it will be interesting to isolate the active chemical constituents which are responsible for the cardiotonic activity as well as to determine the possible mechanism of action.

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