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Research Article

COMPARATIVE CARDIOTONIC ACTIVITY OF *HALDINIA CORDIFOLIA* WITH DIGOXIN ON ISOLATED FROG HEART

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ABSTRACT

Haldinia cordifolia (Roxb..) (Rubiaceae) commonly known as Haridru. Phytochemical studies had revealed the presence of tannins, saponins, triterpinoids, alkaloids. Present study was carried out to determine the cardiotonic activity by using infusion of heartwood with different dilutions & compared with cardiotonic activity of digoxin-the life saving cardiotonic. The activity was tested by using isolated frog heart assembly. The present preliminary studies confirm the better cardiotonic activity of *Haldinia cordifolia* than digoxin. Further studies can confirm the reduced toxicity & this will be the advantage of *Haldinia cordifolia* over digitalis. Thus, in future it will be interesting to isolate the active chemical constituents which are responsible for the cardiotonic activity.

Keywords: Cardiotonic activity, Digoxin, *Haldinia cordifolia*, Isolated frog heart

INTRODUCTION

Despite continuing advances in understanding the basic pharmacology of cardiac glycosides, digitalis intoxication remains a common clinical problem. It necessitates research for new nature based drugs which increase cardiac muscle contractility with a broad therapeutic index. The essential organ of the human body i.e. heart when fails to work leads to sudden death. Since the potent cardiotonic drug i.e. the digoxin which is of the plant origin has a long list of ADR and toxicity, it is a need of hour to develop and standardise cardiotonic drugs of herbal origin.[1-8] *Haldinia cordifolia* (Roxb.) (Rubiaceae) commonly known as Haridru. Growing wildly throughout dark forest of India, ascending to an altitude of 1,200 m in western ghats. The plant has been employed for long time in folk therapy. The heart wood of the plant shows a anti-ulcer, antiambic, antimicrobial, antibacterial properties. The leaves of the plant used as antifertility agent. Certain biochemical constituents namely indol alkaloid like adifoline, 10-deoxyadfoline, 10-deoxyadifoline, 3,4,5,7-tetraacetyl quercetin are investgated from heartwood of the plant. The heartwood was claimed to have general cardiotonic activity and we decided to determine the same with the help of isolated frog heart assembly.[10-11]

MATERIALS AND METHODS [125]

Drug: Infusion of *Haldinia cordifolia* (Roxb.) (Rubiaceae)

Chemical: Digoxin, Ringer Solution

Animal: Frog of *Rana tigrina* species were used for the study and those were maintained as per CPCSEA guidelines.

Instruments: Sherington Rotating Drum, Sterling's heart lever

Preparation of infusion

The plant species *Haldinia cordifolia* (Roxb.) belonging to Family Rubiaceae was collected from Malashej Ghat Dist. Pune and authenticated at Botanical Survey of India, Koregaon Park, Pune. One specimen was preserved in Department of Pharmacognosy of our institute for the reference. The heartwood was washed thoroughly to remove adhered material and fine powder was made by using hand grinder. 1gm of powder was mixed with 100ml distilled water with the help of magnetic stirrer for half an hour. The material was filtered through Whatman filter paper no.40 and filtrate was collected. The prepared infusion was diluted with the help of distilled water in varying proportion and labeled as follows,

A1-Undiluted filtrate
A2-1:1 (filtrate: distilled water)
A3-1:2 (filtrate: distilled water)
A4-1:4 (filtrate: distilled water)

All the preparations were evaluated for their cardiotonic activity by using isolated frog heart assembly. The rate and force of heart contraction was determined.

Preparation of digoxin solution

The marketed digoxin ampoules (Sunpharma Ltd.) were obtained from local market. Various different dilutions were made with distilled water and labeled as follows, B1- 25 µg/ml, B2- 50 µg/ml. Above prepared samples were evaluated for their cardiotonic activity and treated as standard.

Preparation of hypodynamic ringer solution[13-14]

Hypodynamic ringer solution was prepared by using standard method. (Table-1)

Table 1: Composition of hypodynamic ringer solution

Sr. No.	Ingredients	Quantity
1.	Sodium chloride (NaCl)	6.5 gm
2	Potassium chloride (KCl)	0.14 gm
3	Calcium Chloride ($CaCl_2$)	0.03 gm
4	Sodium bicarbonate ($NaHCO_3$)	0.2 gm
5	Glucose	2 gm
6	Distilled Water	1000 ml

Evaluation of cardiotonic activity[13-14]

The frog of species *Rana tigrina* was pithed and pinned it 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 put a few drops of hypodynamic frog ringer over the heart. The inferior venacava was traced, put a thread around it and given a small cut in order to insert the venous cannula. The cannula was inserted in the vein and the thread was tied to assure the cannula in place which is in turn connected to a saline bottle containing hypodynamic frog ringer solution. A small cut in one of the aorta was given 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 that is A1, A2, A3, A4, B1 and B2 were administered in different doses viz. 0.1ml, 0.2ml, 0.3ml respectively. The rate and force of heart contraction were noted as given in (Table 2-7, Figure 1-7).

OBSERVATIONS

Fig. 1:

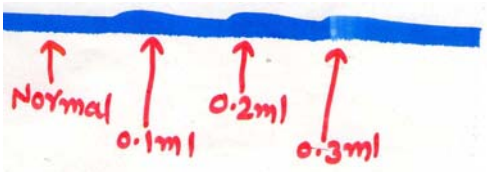


Table 2:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	36	Normal
2	A1	0.1	33	Rapid Increase
3	A1	0.2	29	Slight Increase
4	A1	0.3	25	Increase

Fig. 2:

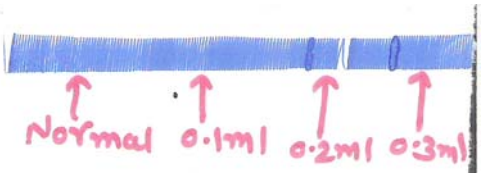


Table 3:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	32	Normal
2	A2	0.1	32	Slight Increase
3	A2	0.2	26	No Change
4	A2	0.3	30	Increase

Fig. 3:

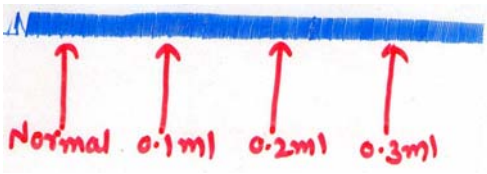


Table 4:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	32	Normal
2	A3	0.1	29	Rapid Increase
3	A3	0.2	27	Increase
4	A3	0.3	28	Increase

Fig 4:

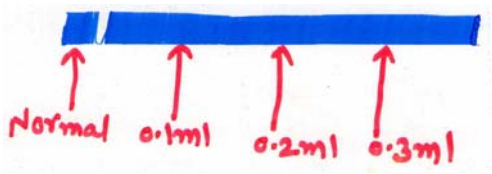


Table 5:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	30	Normal
2	A4	0.1	27	Slight Increases
3	A4	0.2	24	No change
4	A4	0.3	26	No change

Fig. 5:

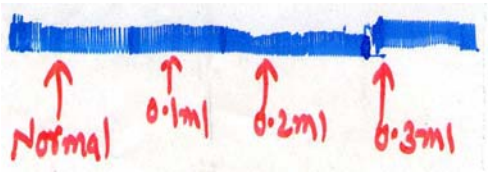


Table 6:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	28	Normal
2	B1	0.1	23	Increase
3	B1	0.2	22	Slight decrease
4	B1	0.3	24	Increase

Fig. 6:

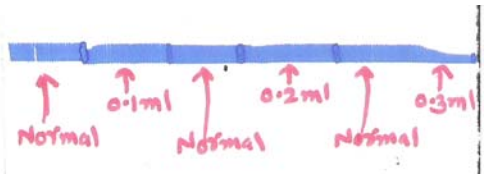


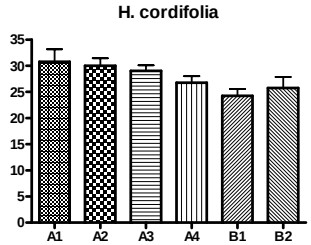
Table 7:

Sr. No.	Drug	Dose(in ml)	Beats/min.	Change in Force
1	.....	Normal	30	Normal
2	B2	0.1	27	Increase
3	B2	0.2	26	Slight Increase
4	B2	0.3	20	Sudden Cardiac Block

RESULTS AND DISCUSSION

All the dilutions of *Haldinia cordifolia* (Haridru) restore cardiac activity of Hypodynamic frog heart i.e. it increases rapidity and force of contraction. It was found that undiluted sample showed better response as compared to other samples. It is interesting to know that *Haldinia cordifolia* (Haridru) has rapid onset of action compared to Digoxin. These preliminary studies confirm the better cardiotonic activity of *Haldinia cordifolia* (Haridru), and it can stand as better option for digitalis. Further studies can confirm the reduced toxicity & this will be the advantage of *Haldinia cordifolia* (Haridru) over digitalis. 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.

Fig. 7:



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