CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1038144

Available online at: http://www.iajps.com Research Article

COMPARATIVE CARDIOTONIC ACTIVITY OF NEEM LEAF EXTRACT WITH DIGOXIN ON ISOLATED FROG HEART

Kranthi Raju Palle*[1]and Shravan Kumar Dholi [2]

[1]*University college of Pharmaceutical Sciences, Satavahana University, Karimnagar.Karimnagar-505001.

[2]Vaageswari Institute of Pharmaceutical Sciences, Beside LMD Police Station, Ramakrishna Colony, Karimnagar, A.P.-505481, India.

Abstract:

Azadirachta indica has been used medicinally throughout history by many different cultures. Many compounds have been found in the exudates of the Azadirachta indica plant that have been used medically by humans. Present study was carried out to determine the cardiotonic activity by using infusion of Neem leafextractwith different dilutions & compared with cardiotonic activity of digoxin-the life saving cardiotonic. The a ctivity was tested by using isolated frog heart assembly. The present preliminary studies confirm the better cardioton ic activity of Neem leaf extract than digoxin. Further studies can confirm the reduced toxicity & this will be the advantage of Neem leaf extract over digitalis. Thus,in future it will be interesting to isolate the active chemical constituents are responsible for the cardiotonic activity.

Keywords: *Cardiotonic activity, Digoxin, Neem leaf extract, isolated frog heart.*

Corresponding author:

Kranthi Raju Palle,

University college of Pharmaceutical Sciences,
Satavahana University,
Karimnagar.Karimnagar-505001.
Email: shravan21m@gmail.com
Mobile: + (91) 8008961562

QR code

*Please cite this article in press as Kranthi Raju Palle et al , **Comparative Cardiotonic Activity of Neem Leaf Extract with Digoxin on Isolated Frog Heart**, Indo Am. J. P. Sci, 2017; 4(10).*

INTRODUCTION:

Herbal products have gained increasing popularity in the last decade, and are now used by approximately 20% of the population. Herbal products are complex mixtures of organic chemicals that may come from any raw or processed part of a plant, including leaves, stems, flowers, roots, and seeds. Although herbs are often perceived as "natural" and therefore safe.[1-2].
Despite continuing advances in understanding
the basic pharmacology of cardiac glycosides, digitali s 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 hu man 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 standardize cardiot onic drugs of herbal origin.
Azadirachta indica can grow into a big tree to a height of about 20 to 35 m. Its canopy of leaves makes it a useful shade tree. It is planted along roads and avenues in the towns and villages of India. It is a tall evergreen tree with the small bright green leaves. It is up to 100 feet tall. It blossoms in spring with the small white flowers. It has a straight trunk. Its bark is hard rough and scaly, fissured even in small trees. The colour of the bark is brown grayish. The leaves are alternate and consist of several leaflets with serrated edges. Its flowers are small and white in color. The edible fruit is oval, round and thin skinned. Several pharmacological activities and medicinal applications of various parts of neem are well known. Biological activity of neem is reported with the crude extracts and their different fractions from leaf, bark, root, seed and oil. However, crude extract of different parts of neem have been used as traditional medicine for the treatment of various diseases. Various parts of the neem tree have been used as traditional ayurvedic medicine in India from time immemorial. The medicinal utilities have been described, especially for leaf, fruit and bark. Neem oil and the bark and leaf extracts have been therapeutically used as folk medicine to control leprosy, intestinal helminthiasis, respiratory disorders, and constipation and also as a general health promoter. Its use for the treatment of rheumatism, chronic syphilitic sores and indolent ulcer has also been evident. Neem oil finds use to control various skin infections1. Bark, leaf, root, flower and fruit together cure blood morbidity, biliary afflictions, itching, skin ulcers, burning sensations and pthysis. However, apart from these uses, there are several reports on the biological activities and pharmacological actions of neem based on modern scientific investigations. [3-4].
The Neem leaf extract was claimed to have general cardiotonic activity and we decided to determine the same with the help of isolated frog heart assembly.

MATERIALS AND METHODS: [5]

Drug: Infusion of Neem leaf extract
Chemicals: Digoxin, Ringer Solution
Animal:
Frog of Rana
Tigrigna 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
Methanolic neem leaf extract was mixed with 100ml distilled water with the help o f 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,
NL1-Undiluted filtrate
NL2-1:1 (filtrate: distilled water)
NL3-1:2 (filtrate: distilled water)
NL4-1:4 (filtrate: distilled water)
All the preparations were evaluated for their cardioto nic activity by using isolated frog heart assembly.
The rate and force of heart
contraction was determined.

Preparation of digoxin solution

The marketed digoxin ampoules (Samarth life sciences Pvt Ltd.) Were obtained from local market. Various different dilutions were made with distilled water and labeled as follows,
D1- 25 µg/ml, D2- 50 µg/ml.
above prepared samples were evaluated for their Card io tonic activity and treated as standard.

Preparation of hypo dynamic ringer solution [6]

Hypo dynamic ringer solution was prepared by using standard Method. (Table-1)

Table1: Composition of hypo dynamic ringer solution

Sr.No	Ingredients	Quantity
1	. Sodium chloride (NaCl)	6.5 gm
2	Potassium chloride (KCl)	0.14 gm
3	Calcium Chloride (CaCl2)	0.03 gm
4	Sodium bicarbonate (NaHCO3	0.2 gm
5	Glucose	2 gm
6	Distilled Water	1000 ml

Evaluation of cardio tonic activity[7]

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 hypo dynamic 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 turnconnected to a saline bottle containing hypo dynamic frog ringersolution. 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 to the hook; it was tied to the free limb of the Sterling's heart attached lever which wasfixed 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 NL1,NL2,NL3,NL4,D1,&D2.were administered in different doses viz. 0.1ml, 0.2ml, 0.3ml respectively. The rate and force of heart contraction [8] were noted as given in (Table 2-7). (Fig-1) (Fig-2).

RESULTS AND DISCUSSION:

All the dilutions of Neem leaf extract 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 Neem leaf extracthas rapid onset of action compared to Digoxin. These preliminary studies confirm the better cardiotonic activity of Neem leaf extract. and it can stand as better option for digitalis.

Further studies can confirm the reduced toxicity and this will be the advantage of G.S over digitalis.

Table-2

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	NL1	0.1	35	Rapid Increase
3	NL1	0.2	30	Increase
4	NL1	0.3	29	Increase

Table-3

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	NL2	0.1	32	Slight Increase
3	NL2	0.2	28	Slight Increase
4	NL2	0.3	29	Increase

Table-4

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	NL3	0.1	30	Rapid Increase
3	NL3	0.2	28	Increase
4	NL3	0.3	28	Slight Increase

Table-5

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	NL4	0.1	30	Slight Increase
3	NL4	0.2	28	Slight Increase
4	NL4	0.3	29	No change

Table-6

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	D1	0.1	25	Increase
3	D1	0.2	24	Slight Increase
4	D1	0.3	26	Slight Increase

Table-7

Sr.No.	Drug	Dose(in ml)	Beats/min	Change in Force
1	-----	Normal	38	Normal
2	D2	0.1	28	Increase
3	D2	0.2	25	Slight Increase
4	D2	0.3	22	Sudden Cardiac Block

CONCLUSION:

Azadirachta indica has been used medicinally throughout history by many different cultures. Many compounds have been found in the exudates of the Azadirachta indica plant that have been used medically by humans. The Neem leaf extract was claimed to have general cardio
tonic activity and we decided to determine the same with the help of isolated frog heart assembly. In conclusion, the leaves of neem acts as for alternative or complementary medicine as a cardio tonic agent.

ACKNOWLEDGEMENTS:

I take this privilege and pleasure to acknowledge the contributions of many individuals who have been inspirational and supportive throughout my work undertaken and endowed with the most precious knowledge to see success in my endeavour.

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