

EVALUTION OF CARDIAC TONIC ACTIVITY OF METHANOLIC LEAF EXTRACT OF *MORINGA OLEIFERA*

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ABSTRACT

The present study was undertaken to evaluate cardio tonic activity of methanolic leaf extract of *Moringa oleifera*. Different parts of the *Moringa oleifera* species are used in India for a wide range of medicinal purposes. Cardio tonic effect of methanolic leaf extract of *Moringa oleifera* was studied by using isolated frog heart perfusion technique (IFHP). Cardio tonic activity was studied on frog isolated heart. Methanolic leaf extract of *Moringa oleifera* as a test and digoxin is used as standard. Present study evaluated three parameters those are force of contraction, heart beats and cardiac output. A significant increased in height of force of contraction (positive inotropic effect) and decreased in heart rate (negative chronotropic effect) and increased cardiac output was observed with the test extract. The present results indicated that a significant increase in height of force of contraction & decreasing heart rates was observed at the lower dose (1mg, 2mg & 4mg) of test extract. At the higher dose (8mg) decreasing contractions. Compared to digoxin, a drug with narrow therapeutic window, *Moringa oleifera* showed wide therapeutic window.

Key Words: Cardio tonic; Hypo dynamic heart; Positive inotropic effect; *Moringa oleifera*. Congestive heart failure

INTRODUCTION

Congestive heart failure occurs when the cardiac output is not adequate enough to meet the demands of the body. This can occur for several reasons, as congestive heart failure is the predominant clinical presentation in multiple disease states.^[1] Heart failure is a common and serious condition associated with high morbidity and mortality^[2]. Chronic heart disease ultimately leads to heart failure (HF), and the incidence of HF increases with age^[3]. Inotropic therapy to enhance cardiac contractile function for HF is still a significant component of the management of HF over decades^[4]. Current inotropic therapy has been associated with increased mortality to various degrees after long-term treatment via a variety of mechanisms, including arrhythmia and apoptosis^[5]. The toxicity of cardio tonic in chronic therapy has hampered the therapeutic value. Thus improvement of inotropic therapy remains one of main aims of the management of HF particularly to the patients who cannot benefit from hemodynamic therapies^[6]. It is generally accepted that the ionic environment of cell profoundly affects the cellular responses of the tissue. For example, the presence of sodium ions in the extracellular medium is necessary for the maintenance of the normal function in a variety of excitable tissues including heart. In several tissues it has been shown that sodium ions may compete with calcium ions, required for excitation-contraction coupling. Cardiac glycosides are still the most important drugs in the treatment of congestive heart failure (CHF). Their exact mechanism of action is unknown, however it is accepted that they finally lead to an increase in the amount of intracellular Ca^{2+} to react with the contractile proteins. In cardiac tissue, the most important regulator of Ca^{2+} homeostasis is sarcoplasmic reticulum (SR), which serves as a sink for Ca^{2+} ions during relaxation and as a Ca^{2+} source during contraction^[7]. Cardiac glycosides produce the positive inotropic action by inhibiting Na-K ATPase pump and hence facilitating the Calcium influx^[8]. It is widely known that a number of inotropic interventions share a common mechanism that governs the availability of Ca^{2+} ions at some sites critical for cardiac contraction.

Cardiac glycosides are a diverse family of naturally derived compounds that bind to and inhibit $\text{Na}^{+}/\text{K}^{+}$ -ATPase. Members of this family have been in clinical use for many years for the treatment of heart failure and atrial arrhythmia, and the mechanism of their positive inotropic effect is well characterized. Exciting recent findings have suggested additional signaling modes of action of $\text{Na}^{+}/\text{K}^{+}$ -ATPase, implicating cardiac glycosides in the regulation of several important cellular processes and highlighting potential new therapeutic roles for these compounds in various diseases.^[9]

Numbers of deaths in industrial world are increasing due to cardiac disease. Cardiac diseases are emerging as single largest contributors for morbidity in India. Cardiac glycosides and catecholamine's are agents of choice in

treatment of congestive cardiac failure (CCF) but cardiac glycosides (e.g. digoxin) have narrow therapeutic index and hence cause many a times intoxication. Despite of the advancement of knowledge in understanding the basic pharmacology of cardioactive drugs glycosides still have its adverse effects in terms of toxication^[10] hence, there is a need for new drug research with wide therapeutic index and good cardiac activity, and by this aim, we have chosen *Moringa oleifera* plant and evaluated its cardioactive potential.

MATERIALS AND METHODS

Standard Drug: Digoxin

Test drug: Methanolic extract of leaves of *Moringa oleifera*

Physiological solutions: Ringer Solution

Animal: Frog (*Rana tigrina*)

Instruments: Sherrington Rotating Drum, Sterling's heart lever

Preparation of extract

The leaves of *Moringa oleifera* was collected from houses at Hanamkonda, Warangal District, Telangana, India. It was authenticated by B.Raju Kakatiya university Warangal district. One specimen was preserved in Department of Pharmacognosy of our institute for the reference. The leaves were 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 proportions.

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

Preparation of digoxin solution Digoxin ampoules (Sun Pharma Ltd.) were purchased from local pharmacy. Various different dilutions were made with distilled water.

Preparation of hypo dynamic ringer solution: Hypo dynamic ringer solution was prepared by using standard method.^[11]

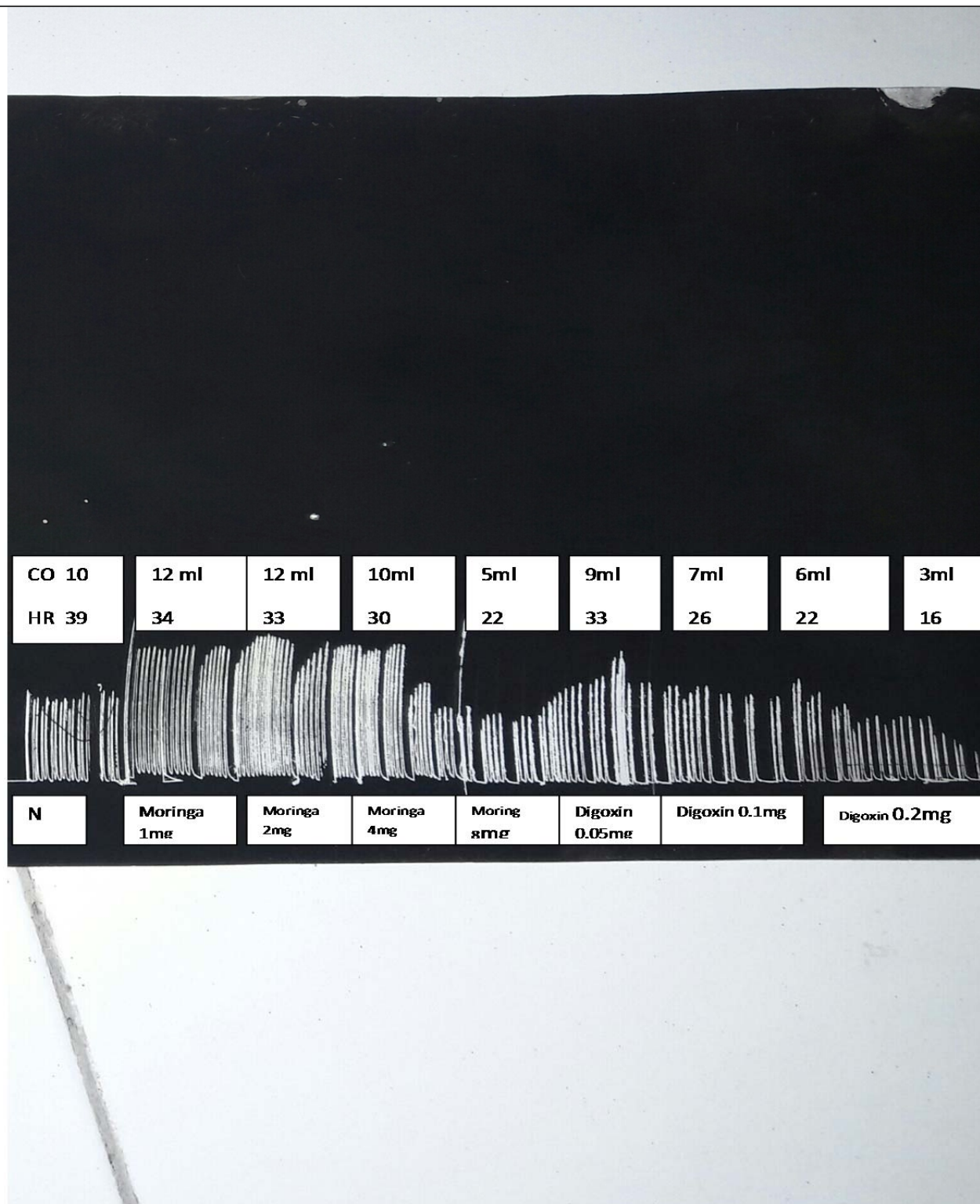
Evaluation of cardio tonic activity The frog of species *Rana tigrina* was pithed and pinned it to the frog board. A midline incision was given on the abdomen, the pectoral girdle was removed and the heart was exposed. The pericardium was carefully removed and put a few drops of hypo dynamic frog ringer 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 turn connected to a saline bottle containing hypo dynamic 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.^[12] The normal heart rate was noted. All test samples that is and standard were administered in different doses 1mg, 2mg, 4mg & 8mg respectively. The rate and force of heart contraction and heart rate were noted as given in the following figures and tables.

RESULTS AND DISCUSSION

Drug	Concentration(mg)	Heart beats	Cardiac output(ml)	Height of the contractions
Normal		39	10	1.6
Moringa oleifera	1	32	10	2.6
Moringa oleifera,	2	29	11	2.4
Moringa oleifera,	4	27	12	2
Moringa oleifera,	8	21	8	1.3
Digoxin	0.05	31	10	1.9
Digoxin	0.1	28	8	1.8
Digoxin	0.2	19	6	1

TABLE 1: CONTRACTION AND HEART BEATS OF METHANOLIC EXTRACT OF MORINGA OLIFERA ON ISOLATED FROG'S HEART

EFFECT OF METHANOLIC LEAF EXTRACT OF MORINGA OLIFERA ON FROG'S ISOLATED HEART



DISCUSSION

Present study described lower doses of test extract give a significant increase in height of contraction. The test extract showed a therapeutic effect in the range of 1-4 mg without any cardiac arrest. Hence, as compared to digoxin, test extract showed wide therapeutic index. (TABLE-1) We all know the adverse effects shown by digoxin and difficulty in its dose adjustments. Also, in the market, there is still no safer alternative for digoxin and it is considered as a sole drug for the treatment of congestive cardiac failure. From the above shown observations, the limitation of using digoxin can be overcome by using the methanolic extract of *Moringa oleifera* leaves which has been found to have excellent cardio tonic activity with the wide therapeutic index as compared to digoxin. Hence, test extract can be a safe alternative to digoxin in congestive cardiac failure.

CONCLUSION

The current study reveals that the methanolic extract of *moringa olifera* possesses good cardio tonic activity. *Moringa olifera* shows therapeutic effect between the 1-4mg without any cardiac arrest. Hence as compared to digoxin test extracts showed wide therapeutic index. But here evaluated force of contractions, heart beats and cardiac output. Regarding these three parameters *Moringa olifera* shows good cardiac tonic activity than digoxin. Digoxin not only used in congestive heart failure, also used in many other diseases like atrial fibrillation. So present study will not exact say moringa has good cardiac tonic activity than digoxin in all diseases. Further studies necessary to evaluate different parameters in various diseases.

REFERENCES

- [1] Jessup M and Brozena S. Heart Failure. *N Engl J Med*. 2003; doi: 10.1056/NEJMra021498.
- [2] Satoskar R S, Bhandakar S D & Nirmala N Rege. Hand-book of pharmacology and pharmacotherapeutics, Revised 19th edition, 435, 2005.
- [3] Scaolz H. Über die Wirkung von calcium und natrium auf die kaliumkon treklur isolierter Meer schwein chenvorhofe. *Pflügers Arch* 1969; 308: 315-332
- [4] Shin T.Y, Jeong H.G, Kim D.K, Kim S.H, Lee J.K. Inhibitory action of water soluble fraction of *Terminalia chebula* on systematic and local anaphylaxis.
- [5] Journal of Ethno pharmacology 2001; 74, 133– 140. Singh C. *Photochemistry* 1990; 29, 2348-2350.
- [6] Stevenson L.W. Inotropic therapy for heart failure. *N. Engl. J. Med* 1998; 339, 1848–1850.
- [7] Stump G.L, Wallace A.A, Gilberto D.B, Gehret J.R, Lynch. Arrhythmogenic potential of positive isotropic agents. *Basic Res. Cardiol.* 2000; 95, 186– 198.
- [8] Thiripathi K D. Cardiac glycosides and drugs for CHF, *Essentials of Medical Pharmacology*, 4th edition (Jay-pee Brothers Medical Publishers Pvt. Ltd. New Delhi), 497, 2002
- [9] Department of Laboratory Medicine and Pathobiology, University of Toronto, Banting Institute, 100 College Street, Room 110, Toronto, Ontario M5G 1L5, Canada.
- [10] Samuel Lunenfeld Research Institute and Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, 6th Floor, 60 Murray Street, Toronto, Ontario M5T 3L9, Canada.
- [11] Moussa ND, Mariko U, katsumata S, Sato S, Suzuki K, 2007; Preventive effects of *Moringa Oleifera* on Hyperlipidemia and Hepatocyte Ultra structural changes in Iron Deficient rats. *Biosci. Biotechnology. Biochem*; 71(8):1826-2833.
- [12] Coelho JS, Santos ND, Napoleão TH, Gomes FS, Ferreira RS, Zingali RB, Coelho LC, Leite SP, Navarro DM, Paiva PM. Effect of *Moringa oleifera* lectin on development and mortality of *Aedes aegypti* larvae. *Chemosphere*. 2009; 77(7):934-8.