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Evaluation of Cardiovascular Activity of an Ayurvedic Product 'Mrityunjay' in Rat Model

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Abstract

Ayurvedic system of medicine is a major component of indigenous systems of medicine in Bangladesh. We used an Ayurvedic drug 'Mrityunjay' which is traditionally used for high blood pressure, heart diseases and heart-quake. We measured the electrocardiographical (ECG) parameters using an ECG machine (Vet 300, EDAN, China) in rat model before and after administration of the test drug. We observed that, Mrityunjay at high doses (800 µg/Kg, 1600µg/kg, 3200µg/kg) produced heart blocks and other arrhythmias, but in normal dose (200µg/Kg) it has no serious untoward effects on cardiac muscle.

Key words: Ayurvedic, Mrityunjay, ECG, Cardiovascular disease, Ketamine.

Introduction

Ayurvedic system is one of the oldest systems of medicines, which has been practiced in this subcontinent for over 3000 years. Ayurveda meaning the science of life, is rooted in the social during the period 600 BC to 700 AD (Ghani, 2005). It is a medical system that deals not only with body but with the mind and spirit as well. According to Ayurveda, most diseases connected with the psychophysiologic and pathologic changes in the body are caused by imbalance in three different dosha (i.e. vata, pitta, and kapha). The fundamental aim of Ayurvedic therapy is to restore the balance between these three major body systems. Any imbalance can lead to inflammation (also called sopha) (Chopra and Doiphode, 2002; Garodia *et al.*, 2007). This balance is necessary for contentment and good health. Ayurveda stresses the use of plant-based medicines. Hundreds of plant-based medicines are employed, some animal products may also be used. Ayurvedic formulations are consider to be safe and more effective in comparison to allopathic formulations which have more side effects (http://en.wikipedia.org/wiki/ Ayurveda). But there is not enough scientific evidence to support such claims.

Mrityunjay is a liquid Ayurvedic drug and it is used as an excellent tonic for high blood pressure, heart diseases and heart-quake. Its manufactured as a liquid preparation from arista process in which the main ingredients are khadira kashtho (*Acacia catechu*), arjun (*Terminalia arjuna*), nageshwar (*Mesua ferre*), brongo (*Belleric myrobalan*), amlaki (*Emblica Officinalis*), bohero (*Terminalia belerica*), shotomuli (*Asparagus*), jotamangshi (*Spikenard*), rasna (*vanda roxburghii*), jostimodhu (*Glycyrrhiza glabra)*, alkushi, Indian long pepper, kakali (*Roscoea Purpurea*) etc., (Bangladesh National Formulary of Ayurvedic Medicine, 1992). The major active ingredients in Mrityunjay are epicatechin, atzelchin, gallonchin, kaempferol, triphala, phenolic acids, flavonoids and tannins. Arjun bark is rich in saponnins, natural anti-oxidants, gallic acid, ellagic acid, oligomeric proanthocyanidins, phytosterols, calcium, magnesium, zinc and copper (http://arjuna.co.in/aboutarjuna.html).

Among the novel instrumental techniques for diagnosis of cardiovascular diseases, ECG remains the most important and commonly used diagnostic procedure as it is noninvasive, easily available and easily repeatable (Erik and Bjarne, 1991). ECG tracings were analyzed following our previous paper (Amran *et al.*, 2008)

The main objective of our study is to investigate the therapeutic efficacy of the Ayurvedic medicines available in Bangladesh using rat model.

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Materials and Methods

Drug: Mrityunjay was purchased from Sree Kundeswari Aushadhalaya Ltd., Chittagong, Bangladesh, It was presented as 500 mL in glass bottle.

Instrument: ECG machine (Edan Vet ECG 300, China) with six channels.

Animals: A total of 100 rats of either sex, weighing about 130-150g, aged about 2 month, were purchased from animal house of Department of Pharmacy, Jahangirnagar University. All the rats were acclimatized to new environment for a period of one week. During the experiment period the rats were kept in a well ventilated animal house at 25^0C. They were supplied with standard pellets and fresh drinking water. All the rats were kept in cage and maintained with natural 12h light and dark cycle.

Anesthetic process: For anesthesia rats were given Ketamine at a dose of 50mg/kg as intramuscular injection.

Machine setup: The electrode wires were connected to the left arm, right arm, left leg, right leg of rib joint. We selected auto option to get rhythm from standard limb lead I, II ,III, avR, avL, avF, V. Finally standard limb lead I and II were used for characterization of ECG.

Calculation of dose: The doses have been calculated from human dose of 10 mL once at a time. The dose calculation was given in the Table 1.

Table 1. Calculation of dose ('X' is body weight).

Concentration (as expressed by "X")	Amount of drug (as expressed by µg/kg)	Action sought
1/16 X	100	Less action
1/12 X	133	Less action
1/8 X	200	Normal action
1/4 X	400	Slight toxic action
½ X	800	Toxic action
X	1600	Toxic action
2 X	3200	Lethal action
4 X	6400	Lethal action
8 X	12800	Lethal action

ECG parameters: Typical ECG tracings are consisted of series of waves that are known as P wave, QRS complex, T wave and U wave. Alongside these, PR interval, RR interval, ST segment, QT interval are also important parameters to identify the abnormalities in the electrical conduction system of the heart. Any disturbance in any of the waves, complexes or intervals indicate some type of arrhythmia or heart disease. These parameters are summarized in Table 2.

Table 2. ECG parameters are summarized in the table 2 (Braunwald 1997; Ganong 2005).

Parameters of ECG	Duration (ms)
P wave	≤100
QRS complex	80-0.110
Q wave	40
R wave	200
S wave	60-100
T wave	160
U wave	80
PR interval	120- 200
ST segment	≤200
R-R interval	600-1200
Q-T interval	350-430

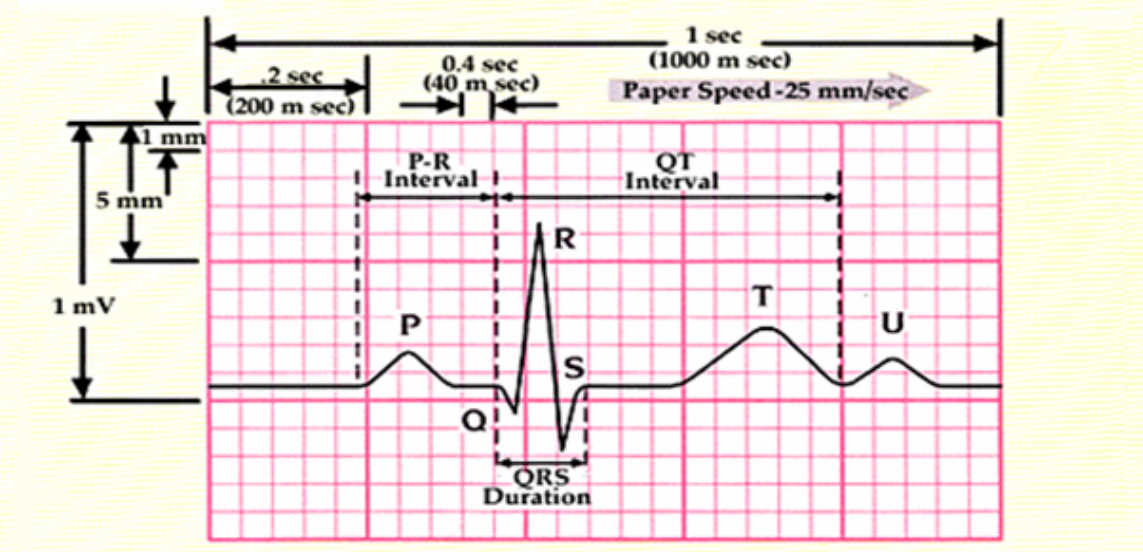
ECG paper speed: The paper moves at a rate of 25 mm/second. Time is measured horizontally. Each small block is 1 mm equal to 0.04 seconds and equal to 0.1 mV. Each bold block is equal to 0.2 seconds. Amplitude is measured vertically.

Results and Discussion

In control mode, the normal heart rate was 208-344 bpm, the range being 250-350 bpm (Figure 2). But when Mrityunjay was administered at a dose of 800µg/Kg, no change in the heart rate was observed (Figure 3) but at a dose of 1600µg/Kg, the heart rate decreased and several types of heart abnormalities were observed (figure 4 'a' and 'b')

After administration of 3200 µg/Kg of the drug, the heart rate was decreased to about 75 bpm. It indicated that Mrityunjay produced a condition looking similar to fibrillation and ultimately leading to the death of the animals (Figure 5).

Data from Auto mode: The auto mode is that mode where heart rate, P wave, PR interval, QRS duration are shown. Using this auto mode we could know about increase or decrease of heart rate. The data obtained after administration of 800µg/Kg were shown in table 3.



Vertical Axis	Horizontal Axis
1 small square = 1mm (0.1 mV)	1 small square = 0.04 s (40 ms)
1 Large square = 5mm (0.5 mV)	1 Large square = 0.2 s (200 ms)
2 Large square = 10mm (1 mV)	5 Large square = 1 s (1000 ms)

Figure 1. Schematic presentation of an ECG tracing **(**Erik and Sigurd, 1991**)**

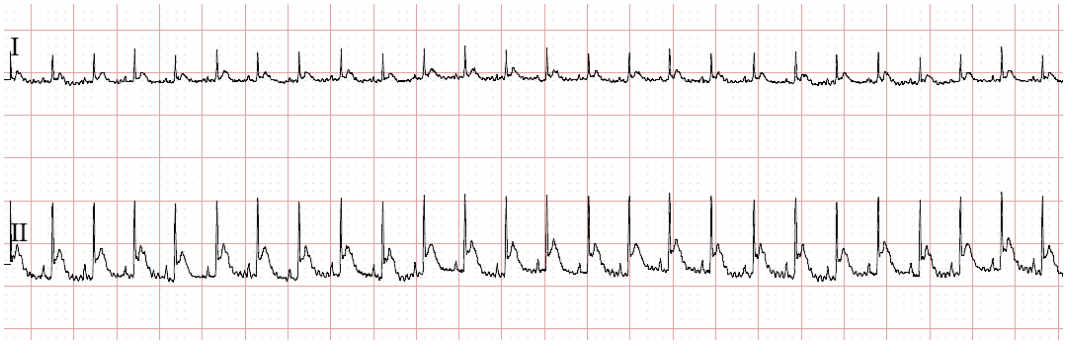


Figure 2. Normal sinus rhythm (NSR) of the rat heart. Only the tracings of the standard limb lead I and II shown. The vertical line indicates milivolt (mV) and the horizontal line indicates time in second (s). The ECG tracings are chosen from one of the ten (n=10) similar and representative experiments.

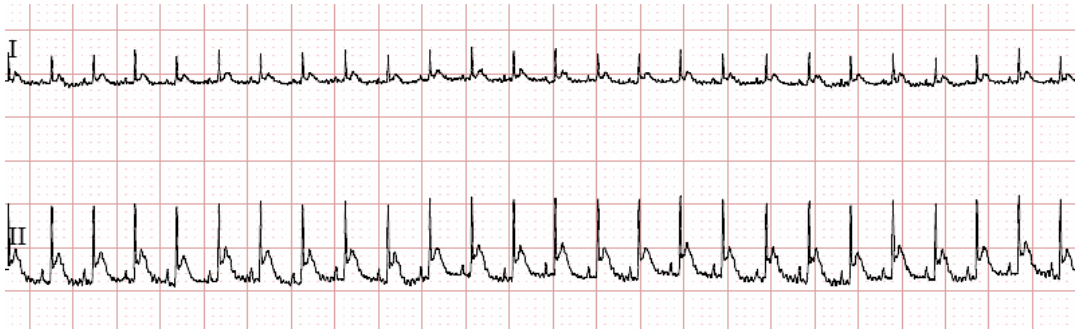


Figure 3. ECG tracing after administration of 800µg/Kg of Mrityunjay. Tracings from limb lead I and II were shown. No abnormalities were found at this dose.

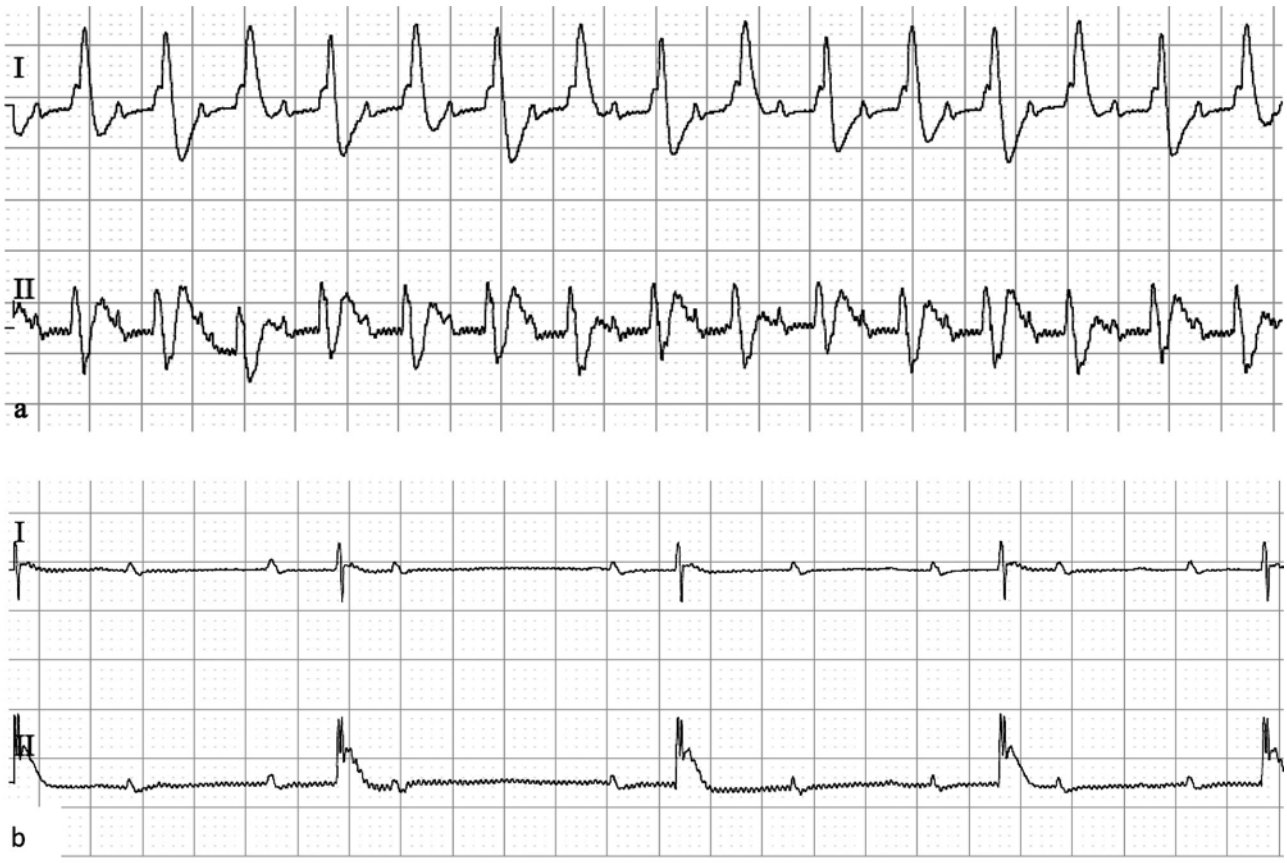


Figure 4. Typical ECG tracings of the standard limb lead I and II after intraperitoneal administration of 1600 µg/Kg of drug. Panel 'a' indicated wide QRS syndrome and panel 'b' indicates both SA nodal and AV nodal blocks. The vertical line indicates mV and the horizontal line indicates time in second (s). The ECG tracings are chosen from one of the (n=10) similar and representative experiments.

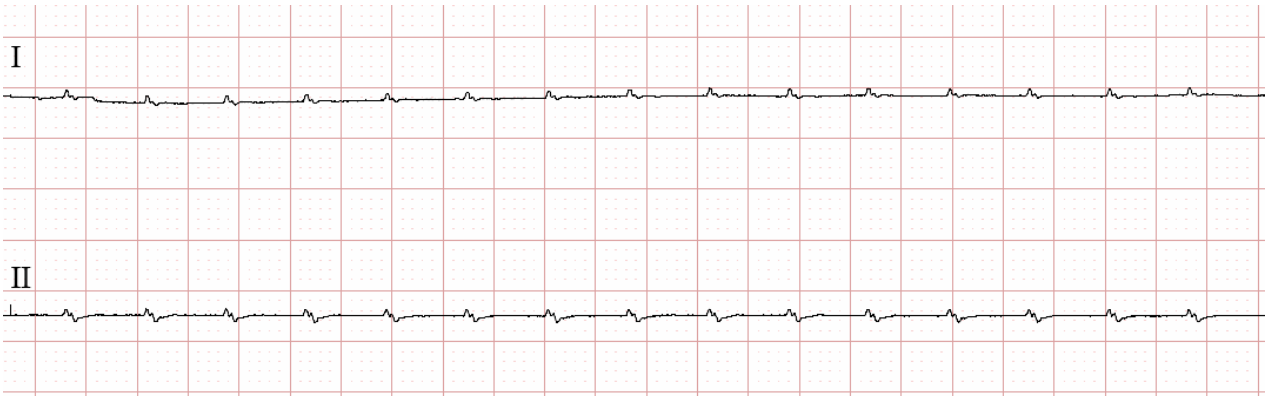


Figure 5. Typical ECG tracings of the standard limb lead I and II after intraperitoneal administration of 3200 µg/Kg of Mrityunjay. Only the tracings of the standard limb lead I and II are shown. Both lead I and II showed fibrillation and dying condition of the animal. The vertical line indicates mV and the horizontal line indicates time in second(s). The ECG tracings were chosen from one of the ten (n=10) similar and representative experiments.

Table 3. Different ECG parameters after administration of Mrityunjay at a dose of 800µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Auto mode.

Time (min)	HR (bpm)	P dur (ms)	PR interval (ms)	QRS dur (ms)
Pretreatment	267.17	37.5	77.17	161.33
10	251.5	44.83	89.83	172.5
15	257..83	44.5	89.83	166.16
20	240.66	58.5	104	187
25	270.17	53.67	94.5	168
30	257.17	43.17	90.33	186
35	256.33	37.6	91.2	143.17
40	276	37	92.6	148.5
45	273.33	39.6	72.4	148.5
50	264	40	73.17	149.17

The data obtained after administration of 1600µg/Kg were shown in the table 4.

Table 4. Different ECG parameters after administration of Mrityunjay at a dose of 1600µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Auto mode.

Time (min)	HR (bpm)	P dur (ms)	PR interval (ms)	QRS dur (ms)
Pretreatment	267.17	37.5	77.17	161.33
10	250.17	37.5	85.17	180.67
15	264	57.25	87.75	153.33
20	254	38	66	125.5
25	271	37.83	70.17	168.17
30	259.33	41.2	102	128.67
35	277.33	33.5	63.75	178.17
40	269	39.5	90.50	135.75
45	199	81.33	115.67	140.25
50	195.5	46.33	101	166.25

The data obtained after administration of 3200µg/Kg were shown in the table 5.

Table 5. Different ECG parameters after administration of Mrityunjay at a dose of 3200µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Auto mode.

Time (min)	HR (bpm)	P dur (ms)	PR interval (ms)	QRS dur (ms)
Pretreatment	267.17	37.5	77.17	161.33
10	273.5	45	64	170
15	302.5	37	58	184.5
20	229.5	77	110	145
25	106.5	98.5	154	171
30	95.5	51	183	118.5
35	106.5	37	156	118
40	67	0	104	104
45	75	0	0	89
50	000	000	000	000

Data from Rhythm mode: the rhythm mode is that mode where lead I, II, III, aVR, aVL, V is located. This mode showed RR avg interval, RR max interval, RR min interval. The data obtained after administration of 800µg/Kg of drug were shown in the table 6.

Table 6. Different ECG parameters after administration of Mrityunjay at a dose of 800µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Rhythm mode.

Time (min)	Total R number	HR (bpm)	RR avg interval	RR max interval	RR min interval
Pretreatment	192.4	241	257.8	540.4	186.25
10	231.8	238.8	255.8	519.4	153.4
15	247.2	249.2	257.8	467.6	192.75
20	218.5	259.5	241.16	420.83	167.6
25	266.2	268.4	235	367.4	160.25
30	245.33	270	231.5	379	182
35	282.2	282	213.4	405.2	195.5
40	264.167	265.5	229.83	344.33	199.5
45	249.83	251.5	242	391.16	188.83
50	251.83	253.33	240.67	318.67	194.33

The data obtained after administration of 1600µg/Kg of drug were shown in the table 7.

Table 7. Different ECG parameters after administration of Mrityunjay at a dose of 1600µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Rhythm mode

Time (min)	Total R number	HR (bpm)	RR avg interval	RR max interval	RR min interval
Pretreatment	192.4	241	257.8	540.4	186.25
10	255	256.83	237.83	399.5	188.33
15	224.83	256.67	237.167	290.67	222.33
20	258.5	258.167	235.67	301.33	218.33
25	287.33	289.83	210.167	250.67	200
30	244	245.67	262.83	465.67	190.67
35	284.75	286.75	213	343	177.75
40	234	249.75	269.75	503.5	250
45	114.25	168.5	698.75	1355.25	611.33
50	190	214	588.75	1312.25	206

The data obtained after administration of 3200µg/Kg of drug were shown in the table 8.

Table 8. Different ECG parameters after administration of Mrityunjay at a dose of 3200µg/Kg. The data are shown as mean of 10 similar experiments (n=10) in Rhythm mode.

Time (min)	Total R number	HR (bpm)	RR avg interval	RR max interval	RR min interval
Pretreatment	192.4	241	257.8	540.4	186.25
10	287	289	213.5	1161	217
15	221.5	223	294.5	1425	205
20	161.5	163	378.5	593.5	164.5
25	92	92	649	1067	510
30	54	54	1102	1200	531
35	32	46	1316.5	2614.5	682
40	48	47	1266	1839	217
45	0000	0	0	0	0
50	0000	0	0	0	0

Conclusion

From the above results and discussion, it can be inferred that Mrityunjay, in normal dose, is a safe drug but it should be used with caution and proper monitoring when higher doses are administered or taken chronically for long time.

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