Available Online at http://www.journalajst.com

ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

ISSN: 0976-3376

Asian Journal of Science and Technology
Vol. 08, Issue, 01, pp.4213-4216, January, 2017

RESEARCH ARTICLE

EFFECT OF AQUEOUS EXTRACT OF *Eclipta alba* ON CADMIUM CHLORIDE INDUCED HYPERTENSION IN WISTAR ALBINO RATS

[1,*]Dr. Ritu Yadav, [2]Dr. Jai Prakash Singh, [3]Dr. Ajay Kumar Sahu and [4]Gaurav Sharma

[1,3]Department of Kayachikitsa, National Institute of Ayurveda, Jaipur, India
[2]Department of Kayachikitsa, IMS, BHU, India
[4]Pharmacologist, Institute of Biomedical Science and Resarch, Jaipur, India

ARTICLE INFO

Article History:
Received 28th October, 2016
Received in revised form
14th November, 2016
Accepted 27th December, 2016
Published online 31st January, 2017

Key words:
Eclipta alba,
Antihypertensive effect,
Amlodipine,
Albino rats.

ABSTRACT

Objective: Hypertension is asymptomatic in nature but produces dreadful effects on the body. The causes, so also the drugs are many & usually the treatment is lifelong. Hence research is going on to find out a suitable & safe drug. Aqueous extract of *Eclipta alba* has been taken to see the antihypertensive effect.

Material and Methods: In the study firstly the hypertension was induced in group 1,2,3,4 by giving $CdCl_2$ 1mg/kg i.p for 15 days. After that group1 was given normal saline, group 2 and 3 was given aqueous extract of *Eclipta alba* at dose 100mg/kg and 200mg/kg twice a day respectively, group 4 was given amlodipine 1mg/kg O.D, The B.P. was measured on day 0^{th} , 15^{th} , 30^{th} ,45^{th} day by non-invasive B.P. system for rodents.

Results: A rise in blood pressure was found on day $15^{th}$of i.p. injection of $CdCl_2$ in all four groups. Group 3 (Aq. Extract *Eclipta alba* at dose 200mg/kg) found have significant changes in, Systolic and diastolic B.P. (119.17 mm/Hg and 80.83 mm/Hg) and also Group 4 (Amlodipine at dose 1mg/kg) found have significant changes in, Systolic and diastolic B.P. (119.83 mm/Hg and 78.00 mm/Hg)

Conclusion: Aqueous extract of *Eclipta alba (*200mg/kg B.D.) was found to posses significant anti hypertension effect in wistar albino rats.

INTRODUCTION

Hypertension (HTN or HT), also known as high blood pressure or arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is persistently elevated (James *et al.,* 2013). Hypertension is common disorder rising in incidence once established treatment is obligatory. It is growing in incidence globally particularly in developing countries (Goldblatt *et al.,* 1934). The WHO rates HTN as one of the most important causes of premature death worldwide (Mackay and Mensah, 2004). A systematic review on the prevalence of HTN in India, for studies published between 1969 and July 2011, reported a range between 13.9 to 46.3% and 4.5 to 58.8% in urban and rural areas of India, respectively (Devi *et al.,* 2013). According to the WHO 2008 estimates, the prevalence of raised BP in Indians was 32.5% (33.2% in men and 31.7% in women) (Noncommunicable diseases country profiles 2011). Only about 25.6% of treated patients had their BP under control, in a multicenter study from India on awareness, treatment and adequacy of control of HTN (Hypertension Study Group Prevalence, 2001).

Corresponding author: Dr. Ritu Yadav
Department of Kayachikitsa, National Institute of Ayurveda, Jaipur, India.

The regional variations (between urban and rural) reported in prevalence of HTN are also seen in cardiovascular diseases. Published literature reports regional variations in mortality and prevalence of CHD and stroke in India (south India has higher CHD mortality and eastern India has higher stroke rates) (Gupta *et al.,* 2012). In an analysis of worldwide data for the global burden of HTN, 20.6% of Indian men and 20.9% of Indian women were suffering from HTN in 2005 (Kearney *et al.,* 2005). The rates for HTN in percentage are projected to go up to 22.9 and 23.6 for Indian men and women, respectively by 2025 (Thankappan *et al.,* 2006). Recent studies from India have shown the prevalence of HTN to be 25% in urban and 10% in rural people in India (Thankappan *et al.,* 2006). Moreover hypertension is multi factorial diseases, accordindly the treatment is diverse. Lots of drugs are already in use either alone or in combinations. Drugs once started usually continued for lifelong. Hence the research is still on to find a safe, cost effective and suitable drug for treatment of hypertension. Apart from conventional allopathic measures, there must be meticulous search for alternative treatment; therefore it is evident to look for natural options & switch on to safer indigenous system of medicine like natural herbs. WHO (in 1980) has also recommended the evaluation of the effectiveness of plants in conditions where there are no safe

modern drugs are available. The animal models of hypertension share many features which are common to human hypertension. The antihypertensive drug discovery and its fruitful outcome are largely dependent on selection of suitable animal model during the preclinical study phase (Pushpendra *et al.,* 2010). $CdCl_2$ induced hypertension is chemical induced hypertension and comes under one of the preclinical scrneening models for hypertension (Pushpendra *et al.,* 2010). Cadmium (Cd) is frequently used in various industrial applications and is a ubiquitous environmental toxicant, also present in tobacco smoke. An important route of exposure is the circulatory system whereas blood vessels are considered to be main stream organs of Cd toxicity. Cadmium chloride ($CdCl_2$) affects mean arterial blood pressure in hypertensive rats. We hypothesized that Cd alters the intracellular calcium transient mechanism, by cadmium-induced stimulation of MAPKs (ERK 1 & 2) which is mediated partially through calcium-dependent PKC mechanism. To investigate this hypothesis, primary cultures of vascular smooth muscle cells (VSMCs) from wistar kyoto (WKY) and spontaneously hypertensive rats (SHR) to exposed to increased concentrations of $CdCl_2$ on cell viability, expression of mitogen-activated protein kinases (MAPKs/ERK 1 & 2), and protein kinase C (PKC) which are activated by Cd in several cell types (Benny Washington *et al.,* 2006). *Eclipta alba* Hassk [Asteraceae] is a small genus of herbs commonly known as *Bringaraja* [Sanskrit].

The plant is distributed throughout India in wet or moist wastelands, ascending upto 2000 m on the hills. Recent study shows its diuretic, hypotensive and hypocholesterolemic effects (Rangineni *et al.,* 2013). Diuretics have been the standard hypertensive drugs over the past 4 decades, though they do not lower BP in normotensives (Tripathi, 2008). These are the drugs which causes a net loss of sodium and water in urine. So diuretics are useful in the treatment of a variety of diseases associated with abnormal retention of salt and water in the extracellular compartments of the body. So the present study was undertaken to investigate the antihypertensive potentiality of *Eclipta alba* on wistar albino rats. *Eclipta alba* has nootropic action (Thakur and Mengi, 2005). So it has relaxant effect on C.N.S. It reduce the H.R. and decrease the B.P. Coumarin compounds present in *Eclipta alba* has Antinociceptive action (Leal *et al.,* 2000). It increase the pain tolerating power of a person and helpfull in reducing stress due to painful stimuli. Thus help in reducing EHT. According to literature no acute toxicity was found at dose 2000mg/kg orally (Tanuja *et al.,* 2013).

MATERIALS AND METHODS

Test sample

2 kg of *Bhringraj* capsule was purchased from Shri Mohta Rasayanshala C-8, 9, Udyognagari, Hathras-204101(U.P.), invoice no 091, batch no 1010525.

Animal

Wistar albino rats with either sex (100-150 gm weight) were used in the study. They were randomly distributed into the groups and housed in cage (6 per cages) maintained under standard conditions at 26±2ºC and relative humidity 44-56% and 12 hr. light; 14 hr dark cycles each day for one week before and during the experiments. All animals were fed the standard rodent pellet diet and water adlibitum (Guide for the care and use of laboratory animals). This project was approved by Institutional Animal Ethical Committee of Institute of Biomedical and Industrial protocol approval no: ibir/iaec/2014/1/2(CPCSEA Registration No: 1737/PO/Rc/S/ 14/CPCSEA) can for the study.

Preparation of animals

The animals were randomly selected, and each animal of respective group marked with picric acid as H (mark on head), B (mark on back), T (mark on tail), HB (mark on head and back), HT(mark on head and tail), BT(mark on back and tail) for individual identification and kept in their cages for 5 days prior to dosing to allow for acclimatization to the laboratory conditions.

Number of animals and dose levels

A total of 30 albino rats were used in the study. These are divided into five groups of six rats each. Hypertension was induced in group 1,2,3,4 by giving $CdCl_2$ 1 mg/ Kg i.p. (intraperitoneal) for 15 days (Badyal *et al.,* 2003). After 15 days on induction of hypertension the groups are treated followingly-

Group 1(n=6)- control group given normal saline and vehicle for one month.
Group 2(n=6)- aqueous extract of *Eclipta alba* at dose 100mg/kg orally B.D for 1 month.
Group 3(n=6)-aqueous extract of *Eclipta alba* at dose 200mg/kg orally B.D for 1 month
Group 4(n=6)-Amlodipine at dose 1mg/kg O.D orally for 1 month.

The dose was decided according to table of Paget and Barns.

Administration of doses

Animals were fasted over night prior to dosing without withholding water. The animals weighed and the test substance was administered in a single dose gavage by an oral feeding needle. Following the substance was administered; food was withheld for a further 3-4 hours.

Evaluation

Body weight, B.P. measurement done by non-invasive B.P. systems for rodents.

BP recording

The instrument used for recording of blood pressure was Non invasive BP instrument for rodents (NIBP system).Volume pressure sensor technology was adopted. Specially designed differential pressure transducer was utilised to measure the blood volume in the tail noninvasively. SBP (systolic blood pressure), DBP (diastolic blood pressure) was measured in each rat. The blood pressure was measured in the conscious state of animals.

Table 1. Effect of therapy in objective parameters in group 1

Groups	Weight (Gm.) Mean ± S.E.M.	Systolic B.P.(mmHg) Mean ± S.E.M.	Diastolic B.P.(mmHg) Mean ± S.E.M.
Group 1	72.33±7.8492	134.33±0.9888	103.33±2.2161
Group 2	81.85±9.0930$^{N.S}$	136.50±1.1762 $^{N.S}$	102.67±2.0602 $^{N.S}$
Group 3	75.40±11.2116$^{N.S}$	119.17±1.3520***	80.83±1.0775***
Group 4	84.77±8.4533 $^{N.S}$	119.83±1.3017***	78.00±1.1547***

N.S= Not Sig.: * P= <0.05; ** P= <0.01; *** P= <0.0001; **** P= <0.00001

OBSERVATIONS AND RESULTS

A rise in blood pressure was found on day 15thof i.p. injection of $CdCl_2$ in all four groups. No significant change in body weight was detected in all test and standard group. Various parameters were subjected to statistical analysis in terms of Mean, Standard Error (S.E.). Software Graph Pad Prism 6 was used and results are calculated by ANOVA test in each group. After one month oral administration of test and standard sample and in statistically comparison between Group 1 Vs Group 2, Group 3 and Group 4 found that Group 2 (*Eclipta alba* at dose 100mg/kg) have not significant changes in weight, Systolic and diastolic B.P.

Group 3 (Aq. Extract *Eclipta alba* at dose 200mg/kg) found have significant changes in, systolic and diastolic B.P. (119.17 mm/Hg and 80.83 mm/Hg)

Group 4 (Amlodipine at dose 1mg/kg) found have significant changes in, systolic and diastolic B.P. (119.83 mm/Hg and 78.00 mm/Hg)

DISCUSSION

Cadmium chloride ($CdCl_2$ 1.0 mg/kg, i.p.) treatment in albino rats for 15 days resulted in elevation of blood pressure. In chronic $CdCl_2$-treated rats blood pressure responses to different doses of *Bhringraj* extract at dose of 100 mg/kg and 200 mg/kg and amlodipine show depressor responses. Systolic and diastolic B.P., significantly decrease in group 3 (*Bhringraj* extract at dose 200 mg/ kg). Treatment with amlodipine (1 mg/kg, p.o.) for one month show depressor responses against systolic and diastolic B.P. in chronic $CdCl_2$ induce Hypertension. Cadmium-induced hypertension and vascular lesion in the kidney of rats fed with subtoxic levels were similar to those found in rats due to partial constriction of one renal artery or some other procedure.

It was shown that the cadmium-induced pressor response as well as hypertension were prevented by calcium channel blockers like amlodipine. It was further suggested that cadmium might mimic calcium ion as a partial agonist or the metal might alter the calcium transport across the cell membrane. In forms of hypertension, it seems that there is alteration in the cation transport which leads to increased blood pressure. Cadmium chloride induced hypertension might be due to the fact that the metal ion might mimic Ca2+ ion as a partial agonist and produce a direct contractile effect on vascular smooth muscle (Al Hashem *et al.,* 2009). Based on the mechanism of hypertension in the $CdCl_2$ hypertensive models, it is suggested that the antihypertensive effects of *Bharangraj* extract might be due to its alteration in the transport of cations across the cell membrane.

Conclusion

The present study shows that *Bhringra* extract *(*200mg/kg B.D.) has a significant antihypertensive effect in $CdCl_2$ induced hypertensive models.

REFERENCES

Al Hashem, F., Dallak, M., Bashir, N., et al. 2009. Camel's Milk Protects against Cadmium Chloride Induced Toxicity in White Albino Rats. *American Journal of Pharmacology and Toxicology,* 4 (3):1074117.

Badyal, K., Lata, H., Dadhich, A.P. 2003. Animal models of Hypertension and effect of drugs, *Indian Journal of Pharmacology.,* 35:3494362.

Benny Washington, Shunta Williams, Patrice Armstrong, Charlie Mtshali, John T. Robinson, and Elbert L. Myles, Cadmium Toxicity on Arterioles Vascular Smooth Muscle Cells of Spontaneously Hypertensive Rats, *International Journal of Environmental Research and Public Health*, 2006, 3(4), 323-328.

Das, S.K., Sanyal, K., Basu, A. 2005. Study of urban community survey in India: growing trend of high prevalence of hypertension in a developing country. *Int J Med Sci.,* 2:70–78 [PMC free article][PubMed]

Devi, P., Rao, M., Sigamani, A., Faruqui, A., Jose, M., Gupta, R., et al. 2013. Prevalence, risk factors and awareness of hypertension in India: a systematic review. *J Hum Hypertens,* 27:281–287

Goldblatt, H., Lynch, Hanzal, R.F., Summerirlleww, study of experimental hypertension:1.Production of persistent elevation of systolic blood pressure by means of renal ischemia, *J Exp Med.,*1934;59:347-79.

Guide for the care and use of laboratory animals, Eighth Edition, National Research Council of the national academics, Washington.

Gupta, R. 1997. Meta-analysis of prevalence of hypertension in India. *Indian Heart J.,* 49:450 [PubMed]

Gupta, R., Guptha, S., Sharma, K.K., Gupta, A., Deedwania, P. 2012. Regional variations in cardiovascular risk factors in India: India Heart Watch. *World J Cardiol*., 4:112–120 [PMC free article] [PubMed]

Hypertension Study Group Prevalence, awareness, treatment and control of hypertension among the elderly in Bangladesh and India: a multicentre study. Bull World Health Organ 2001; 79:490–500[PMC free article] [PubMed]

James, PA., Oparil, S., Carter, BL., Cushman, WC., Dennison-Himmelfarb, C., Handler, J., Lackland, DT., Lefevre, ML., et al. (Dec 2013). "2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)". JAMA 311 (5): 507–20. doi: 10.1001/jama.2013.284427. PMID 24352797.

Kearney, P.M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P.K., He, J. 2005. Global burden of hypertension: analysis of worldwide data. *Lancet*, 365:217–223 [PubMed]

Leal, L.K., Ferreira, A.A., Bezerra, G.A., Matos F.J. and Viana, G.S. 2000. Antinociceptive, anti-inflammatory and Bronchodilator activities of Brazillian medicinal plants

containing coumarin,a comparative study, *J Ethnopharmacol.,* Vol-2, 51-59.

Mackay, J., Mensah, G. 2004. Atlas of heart disease and stroke. Geneva: World Health Organization.

Noncommunicable diseases country profiles 2011. http:// www.who.int/nmh/countries/ind_en.pdf[Accessed 10 May 2013]

Pushpendra K. Sharma, Neeraj S. Vyawahare, Avinash Ladhha, 2010. Preclinical screening models for hypertension in rodents: A review. Pharmacology online 3: 458-472.

Rangineni, V. *et al,* 2013. Diuretic, hypotensive, and hypocholesterolemic effects of Eclipta alba in mild hypertensive subjects: a pilot study. Department of Foods and Nutrition, Post Graduate and Research Center, Acharya NG Ranga Agricultural University, Erragadda, Hyderabad, India. *Indian J Pharm Sci.,* May; 75(3):380-4. doi: 10.4103/0250-474X.117432.

Tanuja, S., Nivedita, S., Anjali, S. 2013. Biochemical and histopathological effects on liver due to acute oral toxicity of aqueous leaf extract of Eclipta alba on female Swiss albino mice. *Indian J Pharmacol.,* Jan-Feb; 45(1):61-65

Thakur,V.D. and Mengi,S.A. 2005. Neuropharmacological profile of Eclipta alba (Linn) *Hassk. J, Ethanopharmacol.,* 26.

Thankappan, K.R., Sivasankaran, S., Sarma, P.S., Mini, G., Khader, S.A., Padmanabhan, P., et al. 2006. Prevalence-correlates-awareness-treatment and control of hypertension in Kumarakom, Kerala: baseline results of a community-based intervention program. *Indian Heart J.,* 58:28–33 [PubMed]

Tripathi, K.D. 2008. Antihypertensive drugs. Tripathi M. Essentials of Medical Pharmacology, 6th ed. New Delhi:Jaypee Brothers Medical publishers (P) LTD, P. 540.

****