Journal Of Harmonized Research (JOHR)

Journal Of Harmonized Research in Pharmacy
6(2), 2017, 24-28

ISSN 2321 – 0958

Original Research Article

EVALUATION OF ANTIHYPERTENSIVE AND ANTIGLAUCOMA ACTIVITY OF *ANDROGRAPHIS PANICULATA* AND *ACACIA ARABICA* USING RAT ANIMAL MODEL.

Md. Salahuddin Ansari* and Pankaj Sharma

Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India 313024.

Abstract: Cardiovascular diseases are the leading cause of death globally. The medicinal value of plants lies in some chemical substances that produce a definite physiological action on the human body. *Andrographis paniculata* is used traditionally as a remedy against common cold, dysentery, cardiovascular disease and *Acacia arabica* is used for the treatment of asthma, cough, and ophthalmic. Hypertension induced by adding 1-2 % NaCl to drinking water for 3-6 months and injecting Deoxycorticosterone acetate-induced (10 mg/kg). Glaucoma is induced in rabbits by intraocular injection of alpha-chymotrypsin. Male rabbits weighing about 2 kg will be pretreated with 10 mg/kg i.p. indomethacin to prevent the otherwise immediate onset of inflammation and then slightly anesthetized with pentobarbital to eliminate any nystagmus. The right eye is anesthetized topically with 2% lidocaine.

The interesting fact is that low dose combination of AP and AEP in highly effecting in decreasing MABP but neither High dose AP nor High dose AEP alone was achieved highest Decrease in MABP. The diabetic rats treated with the EEME (250mg/kg) showed a significant (p<0.05) reduction in fasting serum glucose level as compared to 0 day after 7th, 14th and 21st day treatment. The fall in serum glucose level was gradual and consistent.

Keywords: *Andrographis paniculata*, *Acacia Arabica*, Hypertension, Glaucoma

Introduction: Cardiovascular diseases are the leading cause of death globally[1]. Together they resulted in 17.3 million deaths (31.5%) in 2013 up from 12.3 million (25.8%) in 1990. According to World Health Organization (WHO) more than 80% of the world's populations have full trust on herbal medicine for their primary healthcare needs. Use of traditional medicines in Indian continents represents a long history of human interactions with the environment. The medicinal value of

For Correspondence:
msd_pharma@yahoo.co.in.
Received on: February 2017
Accepted after revision: April 2017
Downloaded from: www.johronline.com

plants lies in some chemical substances that produce a definite physiological action on the human body[2].

Hypertension is the most common disease in industrialized nations, with prevalence above 20 percent in the general population. It imparts an increased risk of stroke, myocardial infarction, heart failure, and renal failure; many clinical trials have shown that reductions in blood pressure reduce the incidence of stroke and myocardial infarction[3].

Andrographis paniculata is used traditionally as a remedy against common cold, dysentery, cardiovascular disease, fever, tonsillitis, diarrhoea, liver diseases, inflammation, herpes and so on[4]. The traditional uses and pharmacological aspects of *A. paniculata* have been well-documented in an extensive review recently[5]. A number of active principles are reported from the plant, which mainly include diterpenoid lactones, flavonoids and polyphenols[6]. However, the prime constituent andrographolide has been mainly attributed for its therapeutic properties. The diterpenoid lactone andrographolide, the principle compound found in A. paniculata, is mainly concentrated in leaves and can be isolated from the crude plant extracts as crystalline solid. The whole herb extract is an effective modality for therapeutic and preventive purposes due to its complex composition and interactions which may modulate signal transduction and metabolic pathway. Though, available preliminary studies indicate its cardioprotective potential in myocardial injury, mechanism involve in cardioprotection remains obscure[7]. The effects of Andrographis paniculata showed increase of the nitric oxide, cyclic guanosine monophosphate, and activity of superoxide and endothelin. The andrographis paniculata as an oxidant to preserve endothelial function; result in maintenance of balance of nitric oxide/endothelin[8]. Also Andrographis paniculata increase blood clotting time, thus pre and post treatment with the extract of this, before angioplasty and after surgery significantly prevented constriction of blood vessels resulting in decreasing risk risk of subsequent closing of blood vessels after angioplasty procedure. Beside the benefits on the surgery Andrographis paniculata found beneficial in myocardial infaction by decreasing the damage of heart muscle and activated fibrinolysis[9]. It shows antihypertensive effects by relaxing the smooth muscle wall of blood vessels consequently resulting in lowering of blood pressure. The cardiovascular activities of crude extract of Andrographis paniculata and andrographolide elucidated that's indicate the significant change in heart rate through alpha adrenoceptors, autonomic ganglion and histamine receptors[10].

Acacia arabica is a multipurpose tree widely distributed in tropical and subtropical countries. It is used by traditional healers for the treatment of asthma, cough, flu, dental carries, fever, diarrhea, and rheumatism and ophthalmic[11]. The use of methanolic extract of *A.acacia* reduces the arterial blood pressure and provides evidence of antihypertensive activities independent of muscarinic receptor stimulation. An aqeous extract of *A.arabica* was also observed that it have sustained dose-related contractile activity on the isolated guinea-pig ileum. Intravenous administration of the extract produced a dose-related significant elevation of blood pressure[12].

Materials and methods: Antihypertensive activity

Deoxycorticosterone (DOCA)-salt hypertension: Hypertension is induced by adding 1-2 % NaCl to drinking water for 3-6 months and injecting DOCA (10 mg/kg) **(Vogel, 2002).**

Age matched Wistar rats of either sex weighing 180–240 g were employed in the present study. The care and the use of these animals were in accordance with the guidelines of the CPCSEA (committee for the purpose of control and supervision of experiments on animals).

Experimental protocol was approved by Institutional Animal Ethics Committee (IAEC)

Deoxycorticosterone acetate-induced (DOCA–salt) experimental HT: DOCA-treated rats were developed HT as previously reported [21]. In brief, a midline abdominal incision was made under anesthesia with a ketamine solution and the left kidney was removed. After 15 days of surgery, administration of DOCA was initiated, twice weekly by subcutaneous injection in a suspension of 0.2 ml of olive oil and drinking water was replaced with 1 % NaCl and 0.2 % KCl [22]. Stable HT develops after 4 week of DOCA–salt administration. The animals were restrained and conditioned for 5 days before commencing blood pressure measurements. The rat tail was heated with 200 W bulb heat lamp for 3–5 min and mean arterial blood pressure (MABP) was recorded using noninvasive blood pressure measurement technique (NIBP-Biopac-MP 100; Goleta, CA, USA). At least three separate indirect pressures were averaged for each animal. The animals having MABP C180 mmHg were considered as a hypertensive [23].

This study consists of seven groups and each group comprises of 5–6 rats of either sex. ALK and AVE 0991 were dissolved in normal saline solution (0.9 %).

Group I (Sham control): rats were underwent sham surgery and were maintained on normal drinking water for whole study period.

Group II (DOCA control): uninephrectomized rats were administered DOCA(20 mg/kg/s.c., twice weekly, 4 weeks) and on 5–6 weeks rats were maintained on normal drinking water without being treated with DOCA.

Group III [high dose AP (Andrographis Paniculata)-treated hypertensive rats]: rats were treated with high dose of ALK (50 mg/kg/i.p.; 9 days) [24], 4-week following DOCA administration.

Group IV [low dose (sub-effective dose) AP-treated hypertensive rats]: rats were treated with low dose ALK (25 mg/kg/i.p.; 9 days), 4-week following DOCA administration.

Group V (high dose AP 0991-treated hypertensive rats): rats were treated with high dose of AVE 0991 (576 lg/kg/i.p.; 9 days) [25], 4-week following DOCA administration.

Group VI (low dose AP-0991-treated hypertensive rats): rats were treated with low dose of AVE 0991(288 lg/kg/i.p.; 9 days), 4-week following DOCA administration.

Group VII (low dose AP - low dose AVE 0991-treated hypertensive rats): rats were treated with low dose ALK (25 mg/kg/i.p.; 9 days) 60 min before treatment with low dose AVE-0991 (288 lg/kg/i.p.; 9 days), 4-week following DOCA administration.

Antiglaucoma activity: Alpha-chymotrypsin induced glaucoma: Glaucoma will be induced in rabbits by intraocular injection of alpha-chymotrypsin.

Male New Zealand rabbits weighing about 2 kg will be pretreated with 10 mg/kg i.p. indomethacin to prevent the otherwise immediate onset of inflammation and then slightly anesthetized with pentobarbital to eliminate any nystagmus. The right eye is anesthetized topically with 2% lidocaine. The anterior hamber will be cannulated with a 30-gauge needle attached to a reservoir set at a pressure of 25 mm Hg. Then a second cannula, 32-gauge, is introduced into the anterior chamber near the limbus and directed to the posterior chamber through the pupil. A sterile isotonic saline solution (0.5 ml) containing 150 units of alpha-chymotrypsin is irrigated through the cannula into the posterior chamber. Care will be taken to avoid the injection of any enzyme into the corneal stroma. Both cannulae are then removed without significant loss of aqueous humor. The eyes will be examined at daily intervals for the first week, then on alternate days for the second week, and then weekly for the duration of the experiments. Intraocular pressure is measured with a tonometer adapted for rabbit eyes. Treatment with plant phytoconstituents will performed before and after surgery **(Vogel, 2002).**

Results and Discussion: Effect of various pharmacological interventions on change in MABP (Mean Arterial Blood Pressure) in deoxycorticosterone acetate (DOCA) treated rats: Effects of pharmacological intervention interventions on MABP in DOCA was observed and found that low dose AP and low dose AEP decrease the blood pressure but not reached to basal level but at High dose AP, High dose AEP and Combination of low dose AP and low dose AEP decrease the blood pressure and reached to basal level. The interesting fact is that low dose combination of AP and AEP in highly effecting in decreasing MABP but neither High dose AP nor High dose AEP alone was achieved highest Decrease in MABP. This result may be due to synergism or additive of low dose AP and low dose AEP.

Table 1 Effect of various pharmacological interventions on change in MABP (Mean Arterial Blood Pressure) in DOCA- treated rats

S. No.	Groups	Decrease in MABP (mm/Hg)	Basal MABP reached
1	Low dose AP	49	No
2	Low dose AEP	45	No
3	High dose AP	78	Yes
4	High dose AEP	81	Yes
5	Combination of low dose AP and low dose AEP	82	Yes

Where AP Is normal extract or Alcholic extract of *Andrographis Paniculata*, where as AEP is Ether extract of *Andrographis Paniculata*.

Effect of Hydroalcoholic extracts of *Andrographis Paniculata* and Metformin on Serum Glucose Level in STZ - Nicotianamide Induced Diabetic Rats.

Streptozotocin - Nicotianamide induced diabetic glaucoma model: Diabetic control rats with no drug treatment showed no significant change in the fasting serum glucose level after 7^{th}, 14^{th} and 21^{st} day as compared to 0 day. The diabetic rats treated with the EEME (250mg/kg) showed a significant ($p<0.05$) reduction in fasting serum glucose level as compared to 0 day after 7^{th}, 14^{th} and 21^{st} day treatment. The fall in serum glucose level was gradual and consistent by 247.60±8.18, 229.00±7.84, 197.40±2.97 after 7^{th}, 14^{th} and 21^{st} day treatment, respectively (Table 6). Diabetic rats treated with Metformin (10 mg/kg) showed consistent fall in serum glucose by 199.60±0.50, 179.40±2.31 and 152.60±3.40 after 7^{th}, 14^{th} and 21^{st} day treatment, respectively. The diabetic rats treated with the EEME (500mg/kg) showed a significant ($p<0.01$) reduction in fasting serum glucose level as compared to 0 day after 7th, 14th and 21st day treatment. The fall in serum glucose level was gradual and consistent by 215.80±3.26, 190.80±2.49, 163.60±2.31 after 7th, 14th and 21st day treatment, respectively.

Table 6. The effects of 3 weeks treatment of ethanolic extracts (250 mg/kg & 500 mg/kg) of leaves of Andrographis Paniculata and of Metformin (10 mg/kg) on serum glucose level in STZ-Nicotianamide induced diabetic rats.

Groups	0 day	7 day	14 day	21 day
Normal Control	83.20±0.96	82.20±0.80	82.80±0.58	85.40±0.67
Diabetic Control	276.20±5.80[b]	274.40±7.30[b]	274.40±8.75[b]	275.00±11.49[b]
STZ-Nicotianamide + Standard	214.40±2.80[b]	199.60±0.50[b]	179.40±2.31[b]	152.60±3.40[b]
STZ-Nicotianamide (EEME 250mg/kg)	258.20±6.62[a]	247.60±8.18[a]	229.00±7.84[a]	197.40±2.97[a]
STZ-Nicotianamide (EEME 500 mg/kg)	240.40±4.20[b]	215.80±3.26[b]	190.80±2.49[b]	163.60±2.31[b]

All values represent means ±S.D. of the mean (n=6),
a = $p< 0.05$; b = $p< 0.01$ vs diabetic control group

Conclusion: On the basis of above study concluded that *Andrographis Paniculata* has potential antihypertensive activity as well as glucose lowering activity. It may be used as alternate natural source of antihypertensive and anti-diabetic agent.

Acknowledgements: Authors are thankful to the Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India-313024 for providing all facilities.

References

1. Shanthi M, Pekka P, and Bo Norrving. World Health Organization. Global Atlas on Cardiovascular Disease. 2011, 3–18.
2. Bethesda MD. NHLBI morbidity and mortality chart book. National Heart, Lung, and Blood Institute. 2002.
3. Garcia CK. Autosomal recessive hypercholesterolemia caused by mutations in a putative LDL receptor adaptor protein. Science 2001;292:1394-1398
4. Lin FL, Wu SJ, Lee SC. Antioxidant, antioedema and analgesic activities of *Andrographis paniculata* extracts and their active constituent Andrographolide. Phytother. Res. 2009; 23: 958–964.
5. Anonymous. Medicinal Plants Research Institute, Department of Medical Sciences. Handbook of Medicinal Plants for Primary Health Care. Text and Journal Corporation, Bangkok; 1990: 38-39.
6. Chiou WF, Chen CF, Lin, JJ. Mechanism of suppression of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide. Br J Pharmacol. 2000; 129(8): 31553-31560.
7. Lesley B. Herbs & natural suppliments: An evidence based guide, second edition. Elsevier Australia. 2007
8. Jarukamjorn k, Nemoto N. Pharmacological Aspect of Andrographis paniculata on health and its major Diterpenoid constituent Andrographolide. Journal of Health Science. 2008, 54 (4) 370-381
9. Bharati BD, Sharma PK, Kumar N, Dudhe R, Bansal V. Pharmacological Activity of *Andrographis Paniculata*: A Brief Review. *Pharmacologyonline 2011(* 2) 1-10
10. Ojha SK, Bharti S, Joshi S, Kumari S, Arya DS. Protective effect of hydroalcoholic extract of *Andrographis paniculata* on ischaemia-reperfusion induced myocardialinjury in rats. Indian J Med Res 2012 March, 135. 414-421
11. Sokeng SD, Koube J, Dongmo F, Sonnhaffouo S, Nkono BL, Taiwe GS, Cherrah Y, Kamtchouing P. Acute and chronic anti-inflammatory effects of the aqueous extract of *Acacia nilotica* (L.) Del. (Fabaceae) pods. Academia Journal of Medicinal Plants 2013 January 1(1): 001-005, ISSN: 2315-7720
12. Zhang C, Kuroyangi M, Tan BK. Cardiovascular activity of 14-deoxy-11,12-didehydroandrographolide in the anaesthetized rat and isolated right atria. Pharmacol Res.1998; 38(6):413–417.
13. Vogel Gerald H. drug discovery and evaluation. Pharmacological assays. springer publication, 2002.