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IMPACT OF NATURAL DIURETICS IN MANAGEMENT OF EYE-INTRAOCULAR PRESSURE AND HYPERTENSION

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ABSTRACT

The present study was undertaken to focus on extraction of the aerial parts of *Dodonaea viscose* (DV) subjected to super critical fluid extraction (SCFE) and evaluation of diuretic, eye-intraocular pressure (IOP) and antihypertensive activities on albino Swiss rats using flame photometry and tonometry respectively. The obtained extract was subjected to column Chromatographic separation using silica gel (100-200 and 60-120 mesh).The extracts and isolated fractions were undergone Phytochemical evaluation, acute toxicity study. Further the extracts and fractions were to evaluate diuretic and intraocular pressure (IOP) activities were performed on dexamethasone (2 mg/kg., i.p) induced hypertension in Wister albino rats as per the OECD and CPCSEA guide-lines. The present results revealed that, DV extract and isolated bio compounds showed excellent diuretic activity, decreases rats eye-IOP and ocular antihypertension activities are highly significant.

KEYWORDS: *Dodonaea viscose*, SCF, IOP, Lipchitz.

INTRODUCTION

Most of natural diuretics like active bio molecules from *Dodonaea viscosa (D*V) indicating for the treatment for cancer, anti-inflammatory, diabetes, neurological disorders, anti-fungal and anti-fertility activity.[1-6] Diuretics are water pills, specially natural diuretics were release excessive Na+ from urine output and also reduces the sodium concentrations from blood i.e. veins and arteries resulting in decrease systolic and diastolic blood pressure. Elevated intraocular pressure is a concerned with hypertension. Imbalances in the production drainage's fluid in eye leads oedema and enhancing the raising of intraocular pressure. This consequences leads to damage the optic nerve and chances of loss of vision based on this criteria our research was concentrated for the prevention loss of vision. Diuretics are the class of drugs that increase the rate of urine flow, however clinically useful diuretics also increase the rate of excretion of N^7a^+ and an accompanying anion, usually, Cl^-. Sodium chloride in the body is the major determinant of extracellular fluid volume and most clinical applications of diuretics are directed towards reducing the extracellular fluid volume by decreasing the total sodium chloride content of the body. A sustained imbalance between the dietary sodium loss is incompatible with the life. A sustained positive sodium balance would result in volume overload with pulmonary oedema and a sustained negative sodium balance would result in volume depletion and cardiovascular collapse. Although, continued administration of a diuretic cause's sustained net deficit in total body sodium, the time course of Natriuresis was finite as renal compensatory mechanisms bring sodium excretion in line with sodium intake, a Phenomenon known as diuretic braking. Furosemides as is used standard drug, for comparison study and to evaluate diuretic and IOP activities.

Extraction

***Supercritical extraction*:**[8] The dried seeds are powdered using a mixer to obtain powder of the raw seeds of *Dodonaea viscosa aerial* (DV) parts. Carbon dioxide (purity 99.99%) as solvent contained in a dip tube cylinder is installed. Supercritical CO_2 was obtained by using SFT-10 Supercritical Fluid Pump. The SFT-10 is a high precision carbon dioxide pump designed to deliver liquid carbon dioxide at pressures up to 10,000 psi (68.9 MPa).

Experimental procedure

Turn on the power to the SFT-110 SFE unit.

Turn on the Peltier cooler at least thirty minutes prior to the start of the experiment.

Powder 50 grams of raw material i.e., dried aerial parts of DV and place the powdered into the SFT-110 Unit's processing vessel and seal. Ensure that both the static/dynamic valve and restrictor valve are closed.

Open the carbon dioxide tank valve to allow the carbon dioxide to come into the unit (~750 psi). Set the oven temperature to 40°C and the restrictor block to 40°C. and set the pressure on the pump to 2000 psi. The pump

should begin to actuate to pressurize the sample vessel. This will take between 12-15 minutes. Once the pressure is up to 2000 psi, allow the sample to “soak” at that pressure for 15 minutes for 40°C.

Open the static/dynamic valve to allow free flow of carbon dioxide through the restrictor valve. Adjust the restrictor valve to achieve about 24ml/min of liquid carbon dioxide. Flow dynamically for 15 minutes. The pump should actuate and continue to maintain sample vessel pressure. Close the static/dynamic valve and allow to “soak” for an additional 15 minutes before repeating the dynamic flow step above. Repeat the static soak and dynamic flow step 5 more times.

Set the vessel temperature to ambient and set the pressure control down to ambient. Allow the unit to vent. When the vessel has reached ambient pressure, disconnect the inlet and outlet fittings, open the vessel and remove the DV powder Similar procedure is carried out by varying the parameters such as temperature (45°C, 50°C and 55°C), pressure (2000 psi, 3000 psi and 4000 psi) and time (20, 25 and 40 minutes). Phytochemical investigations of all extracts were carried out in order to detect the presence of the following class of compounds.

Isolation

Isolation of pure components the isolation of pure components involved the following steps: 1. Chromatographic separation using silica gel (100-200 mesh) 2. Chromatographic separation using silica gel (60-120 mesh). The SFE extract (10 g) was chromatographed over silica gel (100-200 mesh) on column 55 cm length and 6 cm diameter. Elution was carried out with solvent mixtures of increasing polarities. Fractions were collected in 100 ml portions and monitored by TLC (silica gel ‘G’ as adsorbent) and the fractions showing similar spots are pooled together. Elution with ethyl acetate: ethanol (EA: ET-OH) (80: 20) gave brown crystalline solid (450 mg) and named as DVF1.

Phytochemical screening[9]

Phytochemical investigation on seeds extracts of *Dodonaea viscosa* was carried out for the presence of Steroids, Alkaloids, Saponin glycosides, Flavone’s, Cumarins, Tannins and Phenolic compounds, Anthraquinone, and Chalcones, Aurones, Irridoids, Lignans.

Experimental animals

Adult *Wister albino* rats either sex weighing between 150-250 g.

Equipment

The apparatus used for extraction is SFT-110
Company- super critical fluid technologies, Inc,
Newark, DE 19711.302-738-3420
U.S.A (www.supercriticalfluids.com)

Materials and method designs

1. Albino rats weighing 150-250 g of (Wister strain)
2. Tween-80 solution (0.1 %)
3. Stop-Clock
4. Standard drug (Furosemide)
5. Metabolic cage and Measuring jar
6. Tonometer

Acute toxicity was evaluated as per OECD guidelines no.423 of CPCSEA. Therapeutic dose was fixed (600 mg/kg)[10]

Diuretic activity

Diuretics are class of drugs that increase the rate of urine flow, however clinically useful diuretics also increase the rate of excretion of Na^+ and an accompanying anion, usually, Cl^-. Sodium chloride in the body is the major determinant of extracellular fluid volume and most clinical applications of diuretics are directed towards reducing the extracellular fluid volume by decreasing the total sodium chloride content of the body. A sustained imbalance between the dietary sodium losses is incompatible with the life. A sustained positive sodium balance would result in volume overload with pulmonary enema and a sustained negative sodium balance would result in volume depletion and cardiovascular collapse. Although, continued administration of a diuretic cause’s sustained net deficit in total body sodium, the time course of nutriauresis was finite as renal compensatory mechanisms bring sodium excretion in line with sodium intake, a phenomenon known as diuretic braking. Frusemide is a standard drug, used to evaluate diuretic activity.

Experimental the method of Lipchitz *et. al*[11,14] was employed for determination of diuretic activity. Albino rats were randomly divided into 5 groups (n=6) and fasted for 18 hrs with water *ad. libitum* prior to the experiment. Group I received normal saline only served as solvent control (25 ml/kg of the body weight). Group II received Furosemide 20 mg/kg (p.o.) served as a standard. Group III and IV received ethanolic extract of DV of 60 mg/kg and group 5 DVF1 (60 mg/kg, PO) respectively. Immediately after dosing, the rats were placed in metabolic cages (3 in each cages) specially designed to separate urine and faeces. Animals were kept at room temperature of 27± 2°C throughout the experiment. The urine was collected in measuring cylinders up to 5 h after dosing. During this period absolutely avoiding food and water to animals. The total volume of urine collected was measured for all groups. The parameters taken for individual rat were body weight (before and after test period), total urine volume, urine concentration of electrolytes (Na^+, K^+) and pH were applicable. Electrolytes concentration was measured by flame photometry. The results are tabulated in Table 1.

Table 1: Diuretic activity of ethanolic extract of *Dodonaea viscosa* on rats.

Treatment Urine	Volume (ml	Electrolyte Excretion (mEq/Lit) + SEM		pH of Urine	Na+/K+
		Na+ K+	Na+ K+		
I Tween -80 (1%.,p.o.)	1.73 ±0.09	40.8 ±0.7	50.8 ±1.1	8.31 ±0.14	0.98 ± 0.01
II Furosemide (20mg/Kg.,p.o.)	4.92 ±0.10	70.3 ±1.1	58.3 ±1.9	8.02 ± 0.002	1.22 ± 0.06
IIIDV (60mg/Kg.,p.o.)	3.67 ±0.17	51.3±1.3	101.2 ±3.3	8.23 ± 0.004	0.51 ± 0.01
IV DV F1 (60mg/Kg.,p.o.)	1.70 ±0.05	46.7 ± 0.7	53.7 ±1.4	8.29 ± 0.06	0.87 ± 0.01

One way ANOVA followed by Studentized Range Test: $p<0.01$ sig $p>0.05$ NS

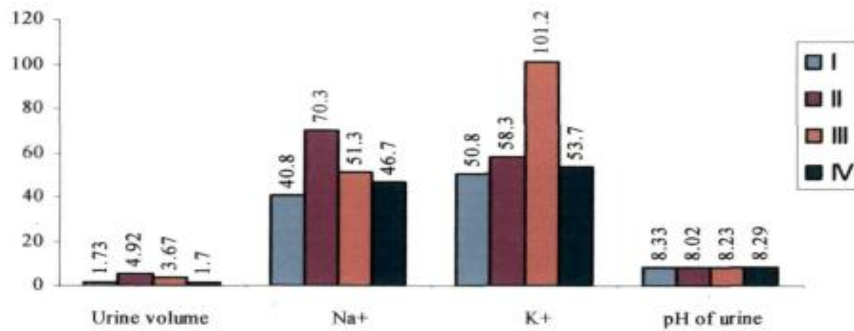

Fig: Diuretic activity of DV extract.

Intraocular Pressure (IOP) experiment Design[15,16]
Intraocular (IOP) pressure is measure in mmHg. Normal ranges from 12-22mm
Hg. If IOP is greater than into be considered higher than normal. Elevated eye pressure might lead to glaucoma. The intraocular pressure assessment protocol as follows:

Group-I received normal saline
Group-II served as DXM (2mg/kg, i.p)
Group III received DXM+ Furosemide (20 mg/kg, i.p)
Group-IV received DXM+DV (SCF-extract 60mg/kg, i.p)
Group-V received DXM+ DVF1 (30mg/kg, i.p)

Table 2: Effect of *Dodonaea* viscosa of bio compounds on intraocular pressure of rats.

Treatment	IOP In time Intervals				
GROUPS	**0min**	**5min**	**10min**	**15min**	**20min**
Normal Saline	15.32	15.02	15.08	15	15.04
DXM (2mg/kg)	19.16	24.08	26.5	28.08	29.3
DXM+ Furosemide(16 mg/kg)	16.23	19.14	18.13	16	15.69
DXM+DV(60 mg/kg)	19.71	22.64	22.13	20.84	19.02
DXM+DVF1(30 mg/kg)	19.92	20.08	19.25	17.89	17.64

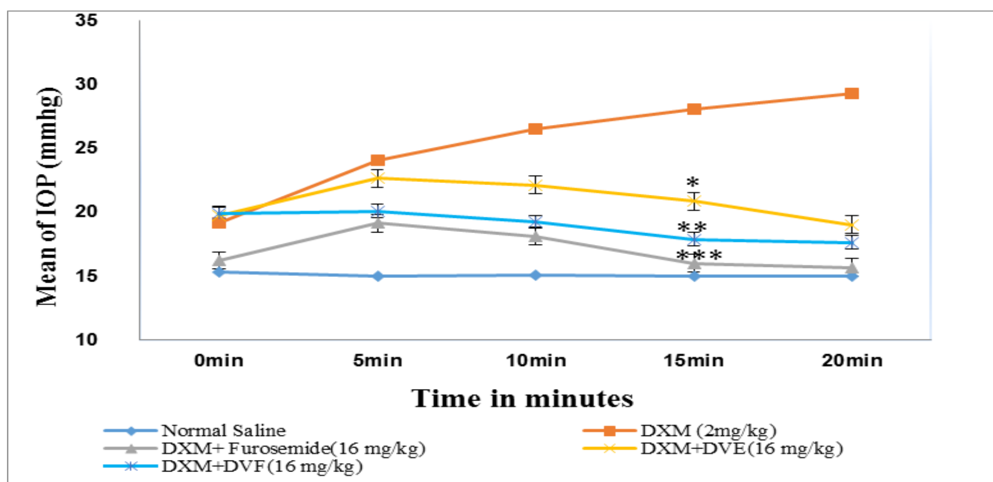

Fig: Showing IOP results of *Dodonaea viscosa*.

RESULTS AND DISCUSSION

The studies on SFC extraction of *Dodonaea viscosa* possess diuretic activity at the dose level of 30 mg/kg dose (P<0.001) of DVF1 as compared to DV 60 mg/kg (Table 1). The constituents responsible for the effect of diuretic activity are not reported so far. The treatment with extract of DV and DVF1at the dose of 30 mg/kg (p.o.) showed increase in K^+ excretion and increase in urine volume. This mechanism is similar phenomena encountered with thiazide[17-20] diuretics of this class enhance the excretion of Ca^{++} and Mg^+ to a certain extent. Thiazide induced increase in excretion of K^+ are most readily for secretion of K^+ are distal to the site of action of thiazides. Hence extract of *Dodonaea viscosa* was probably exhibits similar type of action and acts at same segments of nephrons. Some secondary metabolites usually exhibit diuretic effect. Steroid induced hypertension eve increase in intraocular (IOP) pressure is associated with increased retinal oxidative stress and significant retinal ganglion cells loss-prolonged treatment of DV bio compounds for two weeks as results in normalization of IOP and hypertension. The antioxidant properties of DV might be the factors that contribute to prevention of further loss of preventing retinal ganglion cells and preventing ocular hypertension in dexamethasone induced rats.

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