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High Salt-Induced Hypertensive activity and Evaluation of antihypertensive activity of Sateria glauca in ethanolic extract

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Abstract:
This study sought to assess, using a rat model, the antihypertensive effects of Setaria glauca (SG) ethanolic extract. Hypertension was caused over the course of six weeks by adding 6% NaCl to the diet. Here we divide rats into four groups Group1, Group2, Group3 and Group4, each group having four rats. Group1 was treated with high salt intake in wate and food. Group 2 was exposed with to 6% NaCl and treated with drug telmisartan (Which is an antihypertensive drug 10 mg/kg). Groups 3 and 4 were experimental groups, where hypertension was induced using 6% NaCl, followed by daily oral administration of segregated dose of SG 100 mg per kg and 200 mg/kg body weight respectively for five weeks. The treatment shows significant downfall in blood pressure (pressure <0.05mmHg), heart rate and have diuretic response in hypertensive rats. It shows that the SG effect is dose dependent. These results highlight the potential of SG as an effective antihypertensive agent in managing salt-induced hypertension.

Keywords: Hypertensive, *Sateria glauca* in ethanolic extract, antihypertensive, salt induced, OECD, diastolic blood pressure, systolic blood pressure

Introduction:

High blood pressure, medically referred to as hypertension, is a persistent effect where pressure of blood against the artery walls is elevated. Systolic and diastolic measures are used to evaluate this. The OECD guidelines states that a systolic pressure of more than 140 mmHg and a diastolic blood pressure of more than 90 mmHg are indicative of hypertension. [1]. Blood pressure measurements may be greatly impacted by variables such body size, gender, and age. Often referred to as the "silent killer," hypertension typically presents no noticeable symptoms until it causes damage to vital organs. Research studies

demonstrated effective correlation of cardiovascular illnesses and blood pressure levels. Although effective medications are available, only about one-third animal succeed in maintaining (BP) blood pressure. Research shows that a reduction of just 5 mmHg in systolic blood pressure can decrease overall mortality by 7%, underscoring the importance of exploring additional strategies to manage and lower blood pressure. [2] Although substantial progress has been made in preventing, diagnosing, treating, and managing high BP, it still a major issue. Studies suggest that complementary and alternative medicine (CAM) could provide valuable support in hypertension management. Over the last two decades, there has been a growing acceptance of CAM practices among both patients and healthcare professionals, with herbal medicine emerging as a widely adopted form of alternative therapy globally. Herbal remedies have historically contributed significantly to the discovery and development of modern drugs. However, many plants remain insufficiently studied for their therapeutic potential, possesing immense possibilities for future drug-development [3] ***Sateria glauca*** (Family: Poaceae), commonly referred to as silver grass, is a resilient perennial grass known for its adaptability to various

climates. It typically grows to a height of 1 to 1.5 meters (approximately 3 to 5 feet) and features slender, lance-shaped leaves with a distinct silvery sheen. The plant produces feathery flower spikes that eventually form into small clusters of seeds. Native to Southeast Asia, silver grass has now achieved a global presence, often serving as an ornamental plant and a tool for soil stabilization. Studies have found that Sateria glauca contains a number of biologically active substances that enhance the plant's anti-inflammatory and antioxidant properties, including as flavonoids, tannins, and essential oils. [4] Researchers assessed the antihypertensive effects of Sateria glauca's ethanolic extract on hypertension brought on by a high-salt diet in order to investigate the plant's possible advantages. The study aimed to determine whether the plant's bioactive compounds could contribute to blood pressure regulation, considering its traditional medicinal applications and established antioxidant properties.[5]

Materials and methods:

Drug and chemicals

Every substance, medication, and reagent used in this investigation was of analytical quality. Central Drug House (P) Ltd., Daryaganj, New Delhi provided the ethanol. All test drugs and reagents were freshly prepared prior to each use. Glass-distilled water was used throughout the investigation. Collection of Plant Material.

Plant Material Selection and Collection:

Fresh *Setaria glauca* plants were collected from fields within the army cantonment area in Morar, Gwalior, Madhya Pradesh. The harvested plants were manually crushed, air-dried, and extracted with ethanol using a Soxhlet apparatus for up to eight hours at room temperature. The extract was filtered in two stages first using Whatman filter paper and then with cotton gauze. The filtered solution was freeze-dried, producing a dehydrated extract with an 18% w/w yield. The final extract was stored in a glass desiccator with silicon for further use [6]

Extract Preparation:

A manual grinder was used to mill the Setaria glauca plants into a fine powder after they were cleaned completely with running water, allowed to air-dry in the shade, and then finished with hand grinding. At the Department of Pharmacy at the Shri Ram College of Pharmacy in Banmore, Morena, Madhya Pradesh, India (SRCP), the ethanolic extract was prepared using the soxhlation technique. Using a Soxhlet apparatus, extraction was performed on more than 200 grams of powdered Setaria glauca using ethanol at a concentration of 95%. Eighteen to twenty hours passed throughout the extraction process, which culminated in the appearance of a colorless solvent in the side tube, which indicated that the procedure had reached its end. After that, the solvent was removed by evaporating it in a water bath that was kept at a temperature of fifty degrees Celsius in order to concentrate the extract. The yield percentage of the ethanolic extract was calculated using the original quantity of plant powder that was used. Animal [7] Male albino rats weighing between 160 and 175 grams and aged between 4 and 6 weeks were selected for the aim of this experiment. Additionally, the rats were chosen based on their traits. The animals utilised for scientific study came from SRCP's laboratory animal housing facility. For sixteen hours prior to the experiment, the rats were kept in a metabolic cage. After that, they underwent a week-long acclimatisation phase to help them become used to the environment at the facility. The mice underwent a twelve-hour light-dark cycle while being housed in carefully monitored experimental conditions at a temperature of 25 degrees Celsius. The rats were given a animal laboratory meal and unrestricted access to water.[8] The experiment procedure was authorized through Committee for Institutional Animal Ethics (IAEC) and complied with the guidelines established by the Committee for Control and Supervision of Experiments on Animals (CPCSEA), with CPCSEA No. SRCP/M. Pharm/IAEC/95/23-24.[9]

Induction of hypertension and ethanol extract efficacy test: -

Acclimatised rats received a daily oral dosage of 6% NaCl solution at 1% of their body weight in order to cause hypertension. In order to preserve the individuals' hypertension states, this regimen was followed consistently throughout the research period (7). The animals in the research were divided into four groups, each group four rats. Group I (n = 4)

was given saline water and a high-salt food (6% NaCl) in order to induce hypertension. Group II: standard Treatment The group (n = 4) was treated with 10 mg/kg of telmisartan after being given a high-salt food and salty water. Group III: Test Group 1 (n = 4) consisted of hypertensive subjects receiving treatment with an orally route administration of 100 mg/kg of Setaria glauca ethanolic extract. Group IV: (n = 4) exhibited hypertension followed by receiving an oral treatment of ethanolic plant extract of Setaria glauca on 200mg/kg dose. while adhering to the same dietary regimen. The different parameters such as blood pressure, diuretic response, systolic blood pressure, diastolic blood pressure and heart rate were assessed from start to week five after medical treatment.[10]

Preliminary Screening of phytochemicals: -An investigation was conducted on the potential various phytochemicals contained in the ethanolic extract of Setaria glauca. Alkaloids, flavonoids, tannins, steroids, triterpenes, terpenoids, glycosides, and saponins were all identified using standard analytical procedures (Wagner-Burchard test, Ferric chloride test, Salkowski test, Baljet's test respectively) [11]

Statistical analysis:

The mean ± S.E.M. is used to represent the results. By using approaches like one-way ANOVA and Dunnett's multiple comparison tests with Graph Pad Prism 5 to assess whether the group differences were statistically significant.[12]

Results:

Screening using phytochemicals: The ethanolic extract of the whole Setaria glauca plant contained flavonoids, tannins, steroids, triterpenes, saponins, and glycosides, according to the phytochemical study.[13]

Quantification of water consumed and total volume of urine:

During this research, Wistar rats had a daily water intake of around 26 milliliters and a urine output of 13.16 milliliters over the course of a period of five hours. When treated with telmisartan at 10 mg/kg, rats showed a notable increase in urine output to 18.25 mL, accompanied by a water intake of 30.25 mL. In comparison, administration of When 100 mg/kg of Setaria glauca was administered, it produced a urine output of 14.81 mL and a water intake of 24.6 mL. When the dosage is increased to 200 mg/kg, urine output reached 18.26 mL, with water intake at 31.8 mL. These results point to a dosage-dependent diuretic response, with the 200 mg/kg dose showing the most impact. [14]

Group	Total Urine Vol. (ml/5 Hrs.	Water intake vol. (ml/5Hrs.
Group I (Normal Saline	13.16	26.6
Group II (Telmisartan 10 mg/kg)	18.25	30.25
Group III (*Setaria Glauca* 100 mg/kg)	14.81	24.6
Group IV (*Setaria Glauca* 200 mg/kg)	18.26	31.8

Table: 1 water intake volume (ml) and urine output volume (ml).

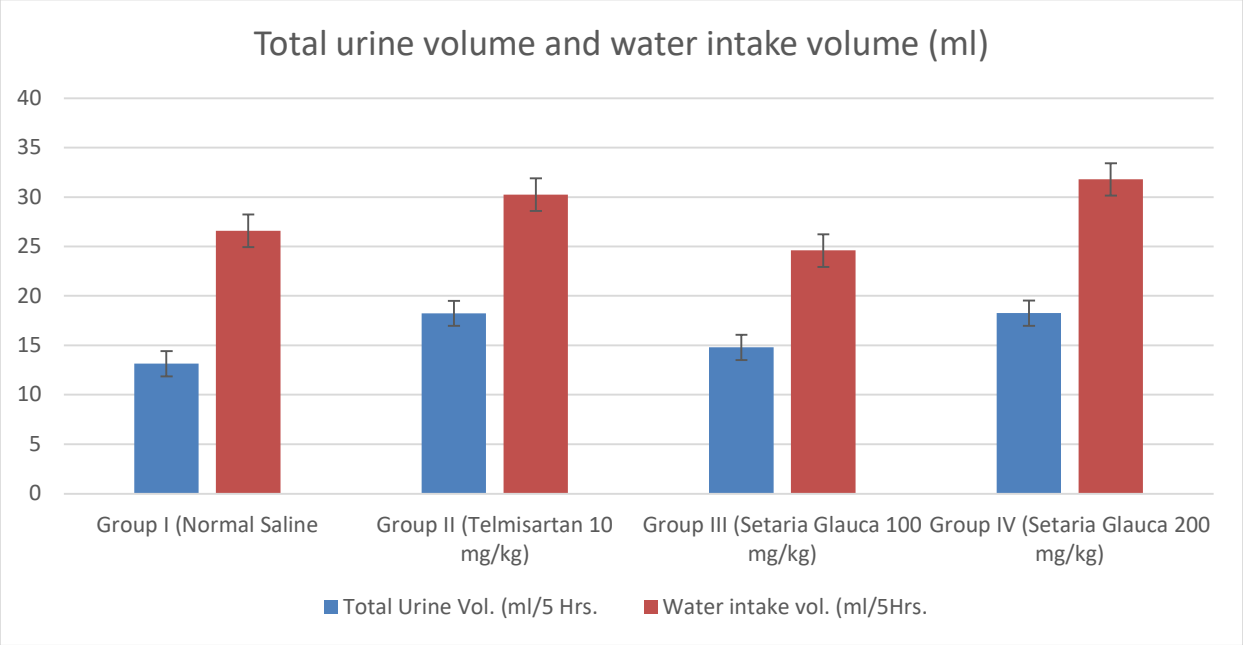

Figure 1: Measurement of total urine volume and water intake volume

Effects of Setaria glauca on Systolic-BP(SBP), Heart Rate (HR), and Diastolic-BP (DBP) in hypertension caused by excessive salt intake After the first five weeks of therapy:

On administering high salt intake shows high heart rate, DBP and SBP in comparison to the disease control group, while administration of 100 mg/kg and 200 mg/kg of Setaria glauca heart rate significantly reverted to normal. Furthermore, Setaria glauca significantly reduced pulse rate, SBP, and DBP in hypertensive rats in a dose-dependent manner when given orally at doses of 100 mg/kg and 200 mg/kg. In similar manner the control animal group on administering 10mg/kg dose of Telmisartan, there is a reduction in SBP and DBP of hypertensive rats.

Table 2: Systolic blood pressure (mmHg)

Group	Week 1	Week 2	Week 3	Week 4	Week 5
Group I (Normal Saline)	140	148	155	165	180
Group II (Telmisartan 10 mg/kg)	130	135	140	150	145
Group III (*Setaria Glauca* 100 mg/kg)	140	145	150	160	155
Group IV (*Setaria Glauca* 200 mg/kg)	135	140	145	155	150

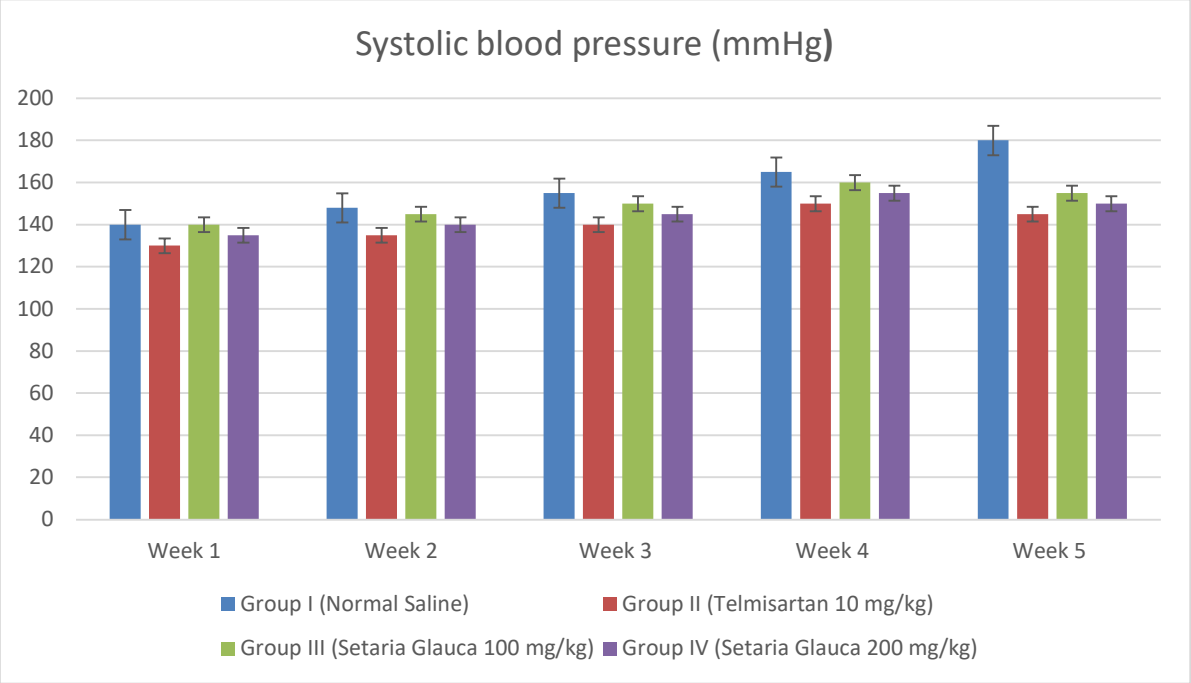

Figure 2: - Effect of SG (*Setaria Glauca)* on SBP in salt-induced hypertensive rats. Results are shown as the average plus or minus the The mean's standard error
(n = 4 for each group). Comparing to *P < 0.05 indicates statistical significance for the control group

Table 3: Diastolic blood pressure in mmHg

Group	**1st week**	**2nd Week**	**3rd Week**	**4th Week**	**5th Week**
Group I (Normal Saline)	100	110	120	135	140
Group II (Telmisartan 10 mg/kg)	95	100	100	110	110
Group III (*Setaria Glauca* 100 mg/kg)	105	105	115	120	125
Group IV (*Setaria Glauca* 200 mg/kg)	100	105	110	115	120

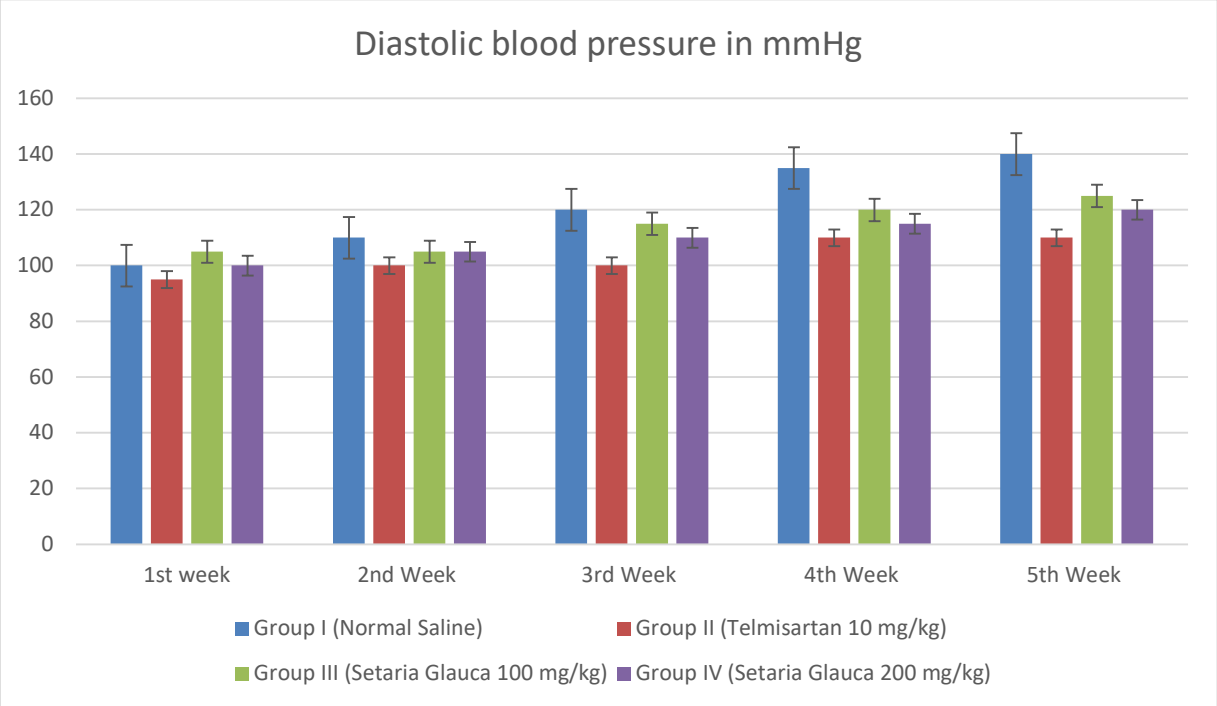

Figure 3: In rats with salt-induced hypertension, the impact of SG (Setaria Glauca) on diastolic blood pressure (DBP) , SBP and Herat rate the mean ± SEM is used to present the data (n = 4 per group).

Table- 4: Pulse Rate (per minutes)

Group	**1 Week**	**2 Week**	**3 Week**	**4 Week**	**5 Week**
Group I (Normal Saline)	450	480	500	550	600
Group II (Telmisartan 10 mg/kg)	400	410	440	400	420
Group III (*Setaria Glauca* 100 mg/kg)	450	455	460	480	510
Group IV (*Setaria Glauca* 200 mg/kg)	430	420	450	430	450

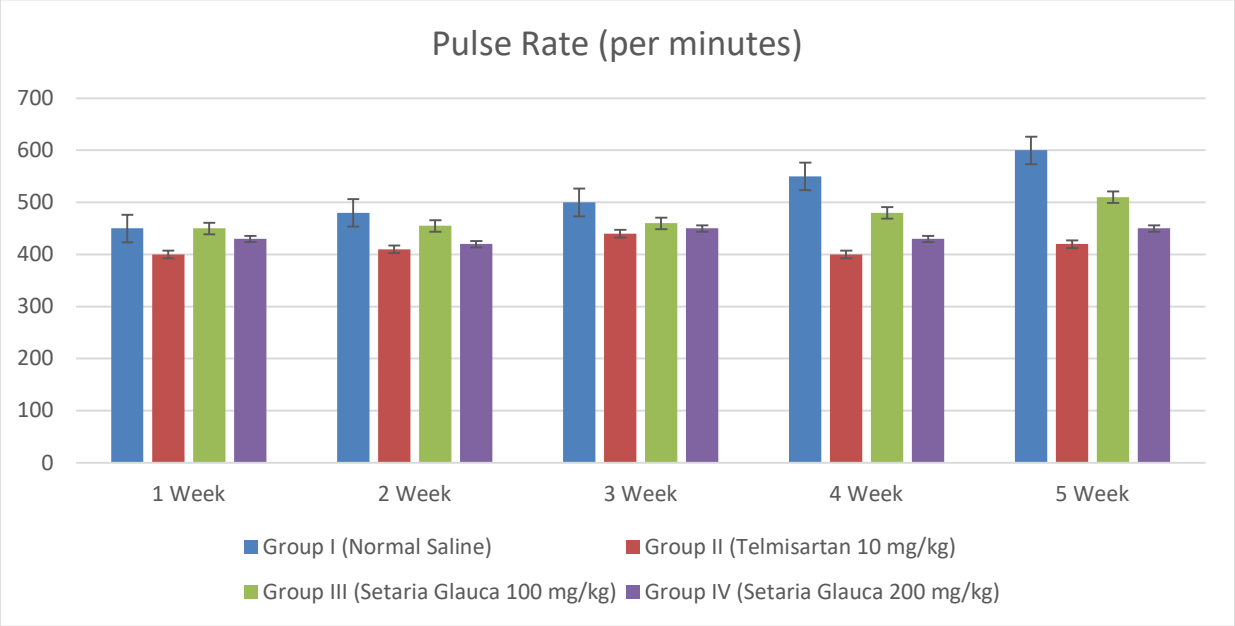

Figure 4: - In rats with salt-induced hypertension, the impact of SG (Setaria Glauca) on pulse rate (beats/min). The data is presented as mean ± SEM (n = 4 per group). When compared to a control group, a P value of less than 0.05 indicates statistical significance.

DISCUSSION:

A chronic condition known as high blood pressure, or hypertension, results in persistently elevated arterial blood pressure.

Two distinct forms of hypertension are: two types of hypertensions: main (essential) and secondary. Primary hypertension represents approximately 90 to 95% of instances, lacking a discernible underlying medical reason [15]. It is common for secondary hypertension, which accounts for between 5 and 10 percent of all instances, to be the consequence of other health problems that affect the cardiovascular system, kidneys, endocrine system, or arteries [16]. Consuming too much high salt dose is hypertension produce most significantly to development of high blood pressure. [17].Numerous epidemiological and genetic investigations consistently show a correlation between high salt consumption and increased blood pressure in rat as compared to normal BP (Prolonged high salt consumption also increases blood pressure in animal models (The mechanisms underlying salt-induced hypertension remain incompletely understood; however, growing evidence indicates that Sodium metabolism is disrupted by genetic abnormalities and polymorphisms in sodium channels and associated kidney proteins., playing a role in salt-sensitive hypertension. These encompass alterations that affect synthesis and circulation concentrations of mineralocorticoids. Since these factors significantly Participate to disruption of BP control and sodium balance inside the kidneys, research into the roles of urinary Swelling, oxidation, and intra-urinary angiotensin effect in salt-produce High BP is still continuing. [18]. Salt-induced hypertension has also been linked to decreased expression of renal VEGF (27). Conventional antihypertensive medications often come with significant side effects. In contrast, around 75–80% For basic healthcare, a large portion of the global population, particularly in less developed nations, uses herbal remedies., owing to their greater tolerability and fewer adverse effects. Over the past three decades, extensive research has focused on identifying indigenous herbal remedies that may possess BP-lowering and hypertension-reducing effects. The initial phytochemical examination indicated that the ethanolic extract of SG is composed of triterpenes, steroids, glycosides, flavonoids, tannins, and saponins. In rats with hypertension brought on by a high-salt diet, the ethanolic extract of Setaria glauca was tested for its ability to reduce blood pressure. Two tested group orally administration SG dose 100 and 200 mg/kg of effects were dose-dependent and resulted in a significant decrease in pulse rate, systolic blood pressure, and Diastolic blood pressure

in hypertensive rats. ethanolic extract of SG dosages of 100 mg/kg and 200 mg/kg, the successfully returned heart rate to normal. Additionally, comparatively [19] to the control group that had generated hypertension, the orally administration of SG dose of 200 mg/kg caused a substantial drop in both SBP and DBP in high BP rats. The presence of bioactive substances including flavonoids and saponins is responsible for the pharmacological effects o ethanolic extraction of SG. The vasorelaxant, anti-hypertensive, and anti-hyperlipidaemic properties of these phytochemicals are well-known.

Conclusion The results demonstrated the effectiveness of SG's ethanolic extract (200 mg/kg) in reducing hypertension in rats that was brought on by a high-salt diet. According to these results, SG may be used as a therapy for hypertension with significant diuretic effects.

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