J Herbmed Pharmacol. 2024; 13(3): 420-426.

http://www.herbmedpharmacol.com doi: 10.34172/jhp.2024.48156

Journal of Herbmed Pharmacology

Diuretic activity and urinary electrolyte effects of *Hemidesmus indicus* (L.) R.Br. & *Decalepis hamiltonii* Wight & Arn. in experimental rats

Sujith Thatipelli[1,2], Ganesan Rethinam[3], Gaddam Dayanand Reddy[4], Shakila Ramachandran[1*], Gopinath Pushparathinam[2*]

[1]Department of Chemistry, Siddha Central Research Institute (Central Council for Research in Siddha, Ministry of AYUSH, Government of India), Anna Hospital Campus, Arumbakkam, Chennai-600106, Tamil Nadu, India

[2]Department of Chemistry, SRM Institute of Science and Technology, Kattankulathur, Chennai-603203, Tamil Nadu, , India

[3]Department of Biochemistry, Siddha Central Research Institute (Central Council for Research in Siddha, Ministry of AYUSH, Government of India), Anna Hospital Campus, Arumbakkam, Chennai-600106, Tamil Nadu, India

[4]Department of Pharmacology, Siddha Central Research Institute (Central Council for Research in Siddha, Ministry of AYUSH, Government of India), Anna Hospital Campus, Arumbakkam, Chennai-600106, Tamil Nadu, India

ARTICLE INFO

Article Type:
Original Article

Article History:
Received: 21 July 2023
Accepted: 1 November 2023

Keywords:
Furosemide
Diuretic activity
Urinary electrolytes
Hemidesmus indicus
Decalepis hamiltonii

ABSTRACT

Introduction: Diuretic drugs are commonly prescribed as primary or adjuvant therapy in various diseases, including congestive cardiac failure and hypertension. However, the adverse effects limit their usage to specific populations. There is an excellent opportunity for drugs with effective diuretic action and limited side effects. The present research was designed to assess the diuretic potential of ethanolic extract of *Hemidesmus indicus* (HIEE) and *Decalepis hamiltonii* (DHEE).

Methods: A total of 8 groups (n=6) of Wistar rats were used in the study to assess the diuretic activity of HIEE and DHEE. Group I was treated with 0.5% carboxymethyl cellulose (CMC), group II with furosemide (10 mg/kg, p.o), groups III-V with HIEE, and groups VI-VIII with DHEE, respectively, at 200, 400, and 800 mg/kg doses. After the treatment, animals were individually shifted to metabolic cages for urine collection at 5 and 24 h intervals and studied the urinary electrolytes. Saluretic and natriuretic effects and the index of HIEE and DHEE were calculated.

Results: The results revealed that both extracts considerably ($P < 0.05$) increased the urine volume and electrolytes (Na^+, K^+, Cl^-) compared to the normal control except low dose treatment. DHEE extract at 800 mg/kg dose showed higher diuretic potential than HIEE in the total volume of urine and urinary electrolytes ($P < 0.05$).

Conclusion: HIEE and DHEE possess diuretic potential, which should be confirmed in human studies.

Implication for health policy/practice/research/medical education:
Hemidesmus indicus and *Decalepis hamiltonii* ethanolic extracts at various doses showed significant diuretic activity. The diuretic potential of *D. hamiltonii* at a high dose (800 mg/kg) was higher than *H. indicus* and hence, *D. hamiltonii* may be considered as potential diuretic drug.

Please cite this paper as: Thatipelli S, Rethinam G, Reddy GD, Ramachandran S, Pushparathinam G. Diuretic activity and urinary electrolyte effects of *Hemidesmus indicus* (L.) R.Br. & *Decalepis hamiltonii* Wight & Arn. in experimental rats. J Herbmed Pharmacol. 2024;13(3):420-426. doi: 10.34172/jhp.2024.48156.

Introduction

Since many centuries, herbal medicines have been used in India to treat or prevent various diseases and for healthy living. Medicinal plants and their derivatives are standard components of Indian indigenous traditional medicinal systems, including Ayurveda, Siddha, and Unani (1). World Health Organization (WHO) accredited the importance of herbal medicines in a notable role in meeting the needs of the population living in rural areas, particularly in developing and underdeveloped countries

***Corresponding authors**: Shakila Ramachandran, Email: r.shakila@gov.in; Gopinath Pushparathinam, Email: gopinath.p@ktr.srmuniv.ac.in

(2). However, the traditional medicinal system is popular and extensively practiced in India to treat or mitigate ailments (3). Medicinal plants have recently gained more interest in developing new drug molecules as they hold pleiotropic pharmacological actions (4). India is one of the world's largest repositories of medicinal plants, and the rural population considers alternative therapeutic systems as the primary treatment choice. However, proper scientific validation of plants and formulations must be screened with modern scientific methods and techniques to convert them into a better choice of drugs (5).

The kidney plays an essential role in maintaining body water content homeostasis, serum electrolytes, blood pressure, and elimination of waste materials and toxins from the body. Diuretics are used in edematous diseases, congestive cardiac failure, and hypertension (6). However, these drugs' chemical nature has adverse effects that may lead to life-threatening conditions, such as hypokalemia, hyponatremia, and acid–base imbalance (7). In spite of the diuretic action of some natural compounds like caffeine, theophylline, and ginger, they have other specific pharmacological effects causing mental confusion and sleeplessness (8). Similarly, some ethno-medicinal compounds have been proven as diuretics in experimental animals (9). Hence, it is necessary to discover novel drugs with potential diuretic activity and fewer side effects that could potentially transform into clinical use prospectively.

Hemidesmus indicus (L.) R. Br., belongs to the family of Apocynaceae and is commonly known as Indian sarsaparilla. Its vernacular names include Sugandhi pala in Telugu, Anantumula and Sugandha in Sanskrit, Nannari in Tamil, and Hindisalsa in Hindi (10). The plant's root has medicinally been used in various Ayurveda and Siddha formulations to treat diseases, including kidney stones and digestive problems. The roots are woody, sweet, and possess a cooling effect, principally used as a diuretic to increase the free flow of urine (11). The known pharmacological activities of *H. indicus* include anti-atherogenic, antispasmodic, memory enhancing, immune-potentiating, and anti-inflammatory activities (12). *Decalepis hamiltonii* is a climbing shrub in the Apocynaceae family and is an indigenous medicinal plant that grows in India's western ghats and Deccan Peninsula (13). In south India and other Asian countries, including Sri Lanka and Indonesia, the roots are used as a locally manufactured health drink Nannari sharbat, which reduces body heat (14). According to the ancient literature, *D. hamiltonii* roots can be used to treat kidney and nutrition disorders (15). *D. hamiltonii* possesses several pharmacological actions, including anti-inflammatory, antimicrobial (16), neuroprotective, hepatoprotective (17), cytoprotective, and antioxidant activities (18). Natural products have played a crucial function in combating human ailments for a long time (19,20). Though HIEE has been used as a coolant and reported with diuretic activity, DHEE has not been reported. Hence, the work was designed to assess the effects of HIEE and DHEE for their diuretic and urinary electrolyte management in experimental rats.

Materials and Methods

Chemicals

Furosemide (CAS Number 54-31-9) was procured from Sigma Aldrich and other analytical grade chemicals from the Merck company.

Collection of plant roots

The roots of *H. indicus* and its adulterant *D. hamiltonii* were collected during summer from Salem District of Tamil Nadu, India. They were authenticated by the Research Officer (Pharmacognosy) of Siddha Central Research Institute and the voucher specimens (D072 and C018 for *H. indicus* and *D. hamiltonii* respectively) were deposited in the herbarium unit.

Preparation of ethanolic extract of *H. indicus* and *D. hamiltonii*

The collected *H. indicus* and *D. hamiltonii* roots were cleaned thoroughly with water and shade-dried. Dried roots were ground to a coarse powder and sieved through mesh number 40. About 5 kg of both plants were soaked with 10 l of 95% ethanol for 48 hours separately, the extracts were filtered, concentrated under reduced pressure using Rota vapor R-300 (Buchi Labortechnik AG Switzerland) to get residue, and stored at -20 °C for further use.

In vivo study

Animals

Both sexes of Wister albino rats (170-220 g) were used in this research. All the animals were housed under standard laboratory conditions in polypropylene cages, with a room temperature of 25±2 °C, relative humidity of 55±5%, and 12 hours light/dark cycle. The animals were allowed to eat standard pellets with drinking water *ad libitum*. The animal experiments were strictly followed the guidelines published by the National Research Council (21). The study was approved by the Institutional Animal Ethics Committee (IAEC).

Experimental schedule

Animals (48 rats) were designated into eight groups, each with six rats. The rats in Group I were treated as the control group and given 0.5% carboxymethyl cellulose (CMC). Group II rats were given furosemide (10 mg/kg body weight). Animals in groups III, IV, and V received HIEE 200, 400, and 800 mg/kg body weight dissolved in 0.5% CMC. Group VI, VII, and VIII animals received DHEE 200, 400, and 800 mg/kg body weight dissolved in 0.5% CMC. All the drugs were administered orally using a rat oral gauge needle.

Analysis of urine

Animals were individually housed in metabolic cages for 24 hours before the experiments for adaptation and training. Immediately after the administration of furosemide, experimental rats were transferred to individual metabolic cages to collect urine. During this period, the food was withheld and drinking water was allowed. Urine samples of individual animals were collected and measured at 5 and 24 hours to calculate the diuretic activity.

The collected urine samples were further used for qualitative analysis like pH, glucose, protein, blood cells, bilirubin, urobilinogen, ketone bodies, nitrites, leucocytes, and hemoglobin (using Urocolor strips Dekaphan Laura, Erba Mannheim, Germany). Similarly, urinary electrolytes, including sodium, chloride, and potassium were estimated (Diestro electrolyte analyzer 103 AP V4, JS Medicina electronica, Argentina), and their indices were calculated as follows:

Ion index = ion concentration in the test group/ ion concentration in the control group

Assessment of diuretic activity and action

The diuretic action was calculated by considering the urine volume in the test and control animals. Diuretic activity was calculated by urine volume in the test and furosemide groups (22).

Natriuretic, saluretic and carbonic anhydrase inhibition (CAI) effects

Calculations were made to assess the saluretic activity by measuring eliminated $Na^+ + Cl^-$. Natriuretic activity was calculated by measuring the ratio of Na^+/ K^+. To evaluate CAI potential, the $Cl^-/ (Na^+ + K^+)$ ratio was computed. A positive natriuretic effect was indicated by values >2.0, while a potassium-sparing effect was indicated by values >10.0 (23).

Statistical analysis

All results were shown as mean ± SEM (n = 6). The data was analyzed by one-way analysis of variance (ANOVA) and Dunnet as post parametric test, analyzed with the software GraphPad Prism 5.0. A P value of <0.05 was defined as statistically significant.

Table 1. Effect of *Hemidesmus indicus* ethanolic extract (HIEE) and *Decalepis hamiltonii* ethanolic extract (DHEE) on urinary pH

Treatment groups	pH
Control (10 mL/kg)	5.91±0.18
Furosemide (10 mg/kg)	8.08±0.13
HIEE (200 mg/kg)	6.93±0.08
HIEE (400 mg/kg)	7.10±0.29
HIEE (800 mg/kg)	7.26±0.29
DHEE (200 mg/kg)	6.83±0.16
DHEE (400 mg/kg)	7.38±0.17
DHEE (800 mg/kg)	7.86±0.24

All data are shown as mean ± SEM with (n=6). The results were analyzed by one-way ANOVA and post-parametric Dunnet test.

Results

Effect of *H. indicus* and *D. hamiltonii* on urinary pH

The urine pH of the control animals was found to be acidic, while furosemide-treated ones gave an alkaline pH. Similarly, both mid and high doses of extracts made the urine slightly alkaline (Table 1).

Effect of *Hemidesmus indicus* and *Decalepis hamiltonii* on qualitative parameters

Effects of HIEE and DHEE on various urine parameters, like specific gravity, glucose, protein, blood cells, bilirubin, urobilinogen, ketone bodies, nitrites, leucocytes, and hemoglobin, were qualitatively tested using a strip method and the results were presented in Table 2.

Effect of *Hemidesmus indicus* and *Decalepis hamiltonii* on urine volume and diuretic activity

The results of HIEE and DHEE on urinary volume, diuretic activity, and diuretic action at 5 and 24 hours of administration were tabulated in Table 3. Animals treated with furosemide showed a considerable ($P < 0.05$)

Table 2. Effect of *Hemidesmus indicus* ethanolic extract (HIEE) and *Decalepis hamiltonii* ethanolic extract (DHEE) on qualitative analysis of urine

Treatment groups	Specific gravity	Glucose	Protein	Blood	Bilirubin	Urobilinogen	Ketone bodies	Nitrite	Leucocytes	Hemoglobin
Control (10 ml/kg)	1	-	0.01	-	-	BDL	-	+	-	-
Furosemide (10 mg/kg)	1.030	-	0.01	-	-	BDL	-	+	-	-
HIEE (200 mg/kg)	1.010	-	0.01	-	-	BDL	-	+	-	-
HIEE (400 mg/kg)	1.005	-	0.01	-	-	BDL	-	+	-	-
HIEE (800 mg/kg)	1.005	-	0.01	-	-	BDL	-	+	-	-
DHEE (200 mg/kg)	1.005	-	0.01	-	-	BDL	-	+	-	-
DHEE (400 mg/kg)	1.030	-	0.01	-	-	BDL	-	+	-	-
DHEE (800 mg/kg)	1.000	-	0.01	-	-	BDL	-	+	-	-

BDL: Below detection limit; -: Absent; +: Present.

Table 3. Effect of *Hemidesmus indicus* ethanolic extract (HIEE) and *Decalepis hamiltonii* ethanolic extract (DHEE) on urine output

Groups	Drug administration					
	After 5 h			After 24 h		
	Urine output (mL)	Diuretic action	Diuretic activity	Urine output (mL)	Diuretic action	Diuretic activity
Control (10 ml/kg)	1.36±0.12	1		3.65±0.21	1	-
Furosemide (10 mg/kg)	3.77±0.09*	2.77	1	7.16±0.13*	1.96	1
HIEE (200 mg/kg)	1.74±0.07	1.28	0.46	3.96±0.12	1.08	0.55
HIEE (400 mg/kg)	2.56±0.07*	1.88	0.68	4.61±0.16*	1.26	0.64
HIEE (800 mg/kg)	2.78±0.13*	2.05	0.74	5.75±0.16*	1.58	0.80
DHEE (200 mg/kg)	1.97±0.07	1.45	0.52	4.51±0.26	1.24	0.63
DHEE (400 mg/kg)	3.03±0.26*	2.23	0.80	5.40±0.17*	1.48	0.75
DHEE (800 mg/kg)	3.25±0.19*	2.39	0.86	6.10±0.17*	1.67	0.85

All data are shown as mean ± SEM with (n=6). The results were analyzed by one-way ANOVA and post parametric Dunnet tests. *P<0.05 compared with the control group.
Diuretic action = Urine output of the test group animals/Urine output of the normal control group animals.
Diuretic activity = Urine output of the test group animals/Urine output of the positive control (furosemide) group animals.

Table 4: Effect of *Hemidesmus indicus* ethanolic extract (HIEE) and *Decalepis hamiltonii* ethanolic extract (DHEE) on the excretion of urinary electrolytes

Groups	Urinary electrolytes (mmol/L)			Index		
	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-
Control (10 mL/kg)	107.2±2.59	61.33±1.62	74.63±3.19	1	1	1
Furosemide (10 mg/kg)	189.2±3.9*	122.6±2.32*	134.0±2.80*	1.764	1.992	1.795
HIEE (200 mg/kg)	123.3±7.92	69.43±2.47	84.16±2.77	1.150	1.132	1.127
HIEE (400 mg/kg)	138.3±2.3*	82.21±1.68*	98.50±4.19*	1.290	1.340	1.319
HIEE (800 mg/kg)	143.7±1.7*	95.93±2.22*	107.7±3.72*	1.340	1.564	1.443
DHEE (200 mg/kg)	131.5±2.01	79.67±2.39	87.00±3.45	1.226	1.299	1.165
DHEE (400 mg/kg)	147.9±2.1*	83.46±1.30*	105.7±2.01*	1.379	1.360	1.416
DHEE (800 mg/kg)	160.1±3.6*	106.0±1.38*	117.5±2.50*	1.493	1.728	1.574

All data are shown as mean ± SEM with (n=6). The results were analyzed by one-way ANOVA and post parametric Dunnet tests. *P<0.05 compared with the control rats.

increase in urine output at 5 and 24 hours compared with the normal control group. Experimental animals administered with HIEE and DHEE increased the urine volume at 400 and 800 mg/kg for both extracts and 200 mg/kg only in DHEE compared with the normal control rats. The diuretic action of high dose (800 mg/kg) of HIEE was double when compared to normal group; however, the mid dose (400 mg/kg) and high dose (800 mg/kg) effects of DHEE were double compared with normal group after 5 hours of drug administration.

Effect of *Hemidesmus indicus* and *Decalepis hamiltonii* on urinary electrolytes excretion

Urinary excretion of electrolytes Na^+, K^+, and Cl^- were increased considerably ($P<0.05$) in the furosemide-treated animals and test drug-treated animals at all doses (200, 400, and 800 mg/kg) compared to the normal control animals (Table 4).

The natriuretic and saluretic effects of *Hemidesmus indicus* and *Decalepis hamiltonii*

HIEE and DHEE significantly exhibited persuasive natriuretic and saluretic effects at all the selected doses compared to the normal group animals (Table 5).

Discussion

Diuretic drugs are essential in managing fluid and salt-associated disorders like hypertension, heart failure, nephrotic syndrome, and edemas. A drug with natriuretic, saluretic, and diuretic action will significantly benefit the treatment (24). A plant with principal bioactive compounds is an essential part of the validation process for the optimal use of its material (25). Diuresis occurs by increasing the output of urine volume and urinary electrolytes. *H. indicus* and its adulterant, *D. hamiltonii,* are widely used in Indian and complementary medicinal systems to treat various diseases, including kidney diseases (11). *H. indicus* and *D. hamiltonii* root extracts are used as a local drink called Nannari during summer as a cooling and flavoring agent (14,26). Exploring the significant biological actions of these plants helps the general public as they are consumed regularly. The present study showed that HIEE and DHEE possess significant diuretic activity. The urine output had increased at 5 and 24 hours after

Table 5. Natriuretic and saluretic effects of *Hemidesmus indicus* ethanolic extract (HIEE) and *Decalepis hamiltonii* ethanolic extract (DHEE)

Groups	(Na^++ Cl^-)	(Na^+/ K^+)	(Cl^-/ [Na^++ K^+])	Index		
				Saluretic	Natriuretic	CAI
Control (10 ml/kg)	181.83	1.75	0.44	1.00	1.00	1.00
Furosemide (10 mg/kg)	323.20	1.54	0.43	1.78	0.88	0.97
HIEE (200 mg/kg)	207.46	1.77	0.44	1.14	1.01	1.00
HIEE (400 mg/kg)	236.80	1.68	0.45	1.30	0.96	1.02
HIEE (800 mg/kg)	251.40	1.49	0.45	1.38	0.85	1.02
DHEE (200 mg/kg)	218.50	1.65	0.41	1.20	0.94	0.93
DHEE (400 mg/kg)	253.60	1.77	0.46	1.39	1.01	1.04
DHEE (800 mg/kg)	277.60	1.51	0.44	1.52	0.86	1.00

CAI: Carbonic anhydrase inhibition.

administration of HIEE and DHEE to experimental animals with the doses of 200, 400, and 800 mg/kg and the diuretic effect showed to be dose dependent. The diuretic action of DHEE (800 mg/kg) was considerably higher than HIEE, indicating the helpfulness of consuming the extract for hypertensive and edematous patients but dehydration and electrolyte loss should be monitored. The present study agrees with Gadge et al results that the HIEE has shown potent diuretic action in rats (24). Similarly, the urinary pH of animals treated with mid and high doses of HIEE and DHEE revealed mild alkaline pH similar to furosemide-treated animals compared to the normal control rats. Alkaline urine helps in eliminating the majority of drugs and favors less formation of urinary calculi (27). Hence, consuming these root extracts as flavoring or cooling agents may protect the kidneys.

The root extracts and furosemide significantly increased the excretion of urinary electrolytes in rats. The diuretic effects of HIEE and DHEE are remarkable and may increase the saluretic and natriuretic effects of extracts. Furosemide possesses a marked diuretic effect by inhibiting the $Na^+/K^+/2Cl^-$ co-transport mechanism of nephrons. Thus, it causes an increase in the elimination of the said urinary electrolytes (28). Our study revealed similar results by the increase of Na^+, K^+, and Cl^- concentrations in urine principally. A high dose (800 mg/kg) of DHEE possessed markable saluretic and natriuretic effect. This indicates the possibility of phytochemical components of both extracts interacting with $Na^+/K^+/2Cl^-$ co-transporter of nephrons to exhibit the diuretic effect.

Hemidesmus indicus and *D. hamiltonii* have many phytochemical substances, such as glycosides, steroids, polyphenols, triterpenoids, and coumarins, which may contribute to the diuretic potential of both plants. In our previous study, the crucial terpenoids lupeol acetate, lupeol, common steroid β-sitosterol, phenolic compounds, such as proto-catechuic acid and ρ-coumaric acid, were screened and a method was developed for their quantification in the *H. indicus* and *D.* hamiltonii root extracts (20). The comparative study revealed that the content of lupeol was found higher in *D. hamiltonii* than *H. indicus,* whereas lupeol acetate was found higher in *H. indicus* than *D. hamiltonii* and ρ-coumaric acid was found only in *H. indicus* and proto-catechuic acid only in *D. hamiltonii*.

On the other hand, HPTLC pattern of *D. hamiltonii* comprised more phyto-compounds with different R_f values that may cling to higher diuretic activity than that of *H. indicus.* Many researchers have revealed that flavonoids, triterpenoids, and other phenolic compounds, like gallic acid, possess diuretic actions (29-32). *D. hamiltonii* reported to have more number of phenolic compounds, such as caffeic acid, protocatechuic acid, gentisic acid, syringic acid, ferulic acid (19), ellagic acid (33), and (2S)-5,7,4-trihydroxy flavanone 4-O-β–d-glucoside (a flavonoid) (34), which are not present in *H. indicus*. This may contribute to higher diuretic activity of *D. hamiltonii* than *H. indicus.* Due to the shortage of *H. indicus* for commercial use, *D. hamiltonii* may be a replacement, with better activity.

Conclusion

The present research concludes that HIEE and DHEE at various doses possess significant diuretic activity within 24 hours. The diuretic effect further enhances the excretion of urinary electrolytes and may help in managing various diseases like hypertension and congestive heart failure. The diuretic potential of DHEE at a high dose (800 mg/kg) was higher than HIEE. However, additional studies are warranted for clarifying their mechanism action. Isolation of more phytochemicals with diuretic effects from *H. indicus* and *D. hamiltonii* Is also recommended.

Acknowledgments

The authors thank the Director General, Central Council for Research in Siddha, and The Assistant Director I/c, Siddha Central Research Institute, SRM Institute of Science and Technology, Kattankulathur, Chennai, for facilities and encouragement.

Author contributions

Conceptualization: Gopinath Pushparathinam.
Data curation: Gaddam Dayanand Reddy.
Formal analysis: Shakila Ramachandran.
Investigation: Sujith Thatipelli.
Methodology: Sujith Thatipelli.
Project administration: Shakila Ramachandran, Gopinath Pushparathinam.
Resources: Ganesan Rethinam.
Software: Ganesan Rethinam, Gaddam Dayanand Reddy.
Supervision: Shakila Ramachandran, Gopinath Pushparathinam.
Validation: Shakila Ramachandran.
Visualization: Shakila Ramachandran.
Writing–original draft: Sujith Thatipelli.
Writing–review & editing: Shakila Ramachandran.

Conflict of interests

The authors declare no conflict of interest.

Ethical considerations

The IAEC of Siddha Central Research Institute, Chennai, approved the study protocol. IAEC Approval Number: IAEC-33/211/Pharma-SCRI/2020.

Funding/Support

The current work received no external funding.

References

1. Nelson VK, Pullaiah CP, Saleem Ts M, Roychoudhury S, Chinnappan S, Vishnusai B, et al. Natural products as the modulators of oxidative stress: an herbal approach in the management of prostate cancer. Adv Exp Med Biol. 2022;1391:161-79. doi: 10.1007/978-3-031-12966-7_10.
2. Petersen PE. Global policy for improvement of oral health in the 21st century--implications to oral health research of World Health Assembly 2007, World Health Organization. Community Dent Oral Epidemiol. 2009;37(1):1-8. doi: 10.1111/j.1600-0528.2008.00448.x.
3. Yuan H, Ma Q, Ye L, Piao G. The traditional medicine and modern medicine from natural products. Molecules. 2016;21(5):559. doi: 10.3390/molecules21050559.
4. Noor F, Tahir Ul Qamar M, Ashfaq UA, Albutti A, Alwashmi ASS, Aljasir MA. Network pharmacology approach for medicinal plants: review and assessment. Pharmaceuticals (Basel). 2022;15(5):572. doi: 10.3390/ph15050572.
5. Aware CB, Patil DN, Suryawanshi SS, Mali PR, Rane MR, Gurav RG, et al. Natural bioactive products as promising therapeutics: A review of natural product-based drug development. S Afr J Bot. 2022;151(4):512-28. doi: 10.1016/j.sajb.2022.05.028.
6. Malhotra M, Ahmed F. Evaluation of blood glucose, kidney function test, electrolytes and vitamin D in chronic kidney disease patients. Eur J Cardiovasc Med. 2023;13(1):856-60.
7. Melka AE, Makonnen E, Debella A, Fekadu N, Geleta B. Diuretic activity of the aqueous crude extract and solvent fractions of the leaves of *Thymus serrulatus* in mice. J Exp Pharmacol. 2016;8:61-7. doi: 10.2147/jep.s121133.
8. Radwan A, Al Jazairi A, Qaddourah N, Ahmed S, Albrahim S, Elhusein B, et al. Caffeine, mental well-being, and psychiatric disorders. In: Mohamed W, Kobeissy F, eds. Nutrition and Psychiatric Disorders. Singapore: Springer; 2022. p. 201-19. doi: 10.1007/978-981-19-5021-6_10.
9. Bhat AH, Sharma HG. Medicinal plants: a potent source of diuretics and antioxidants in traditional medicinal systems. In: Singh A, Singh P, Bithel N, ed. Advanced Pharmacological Uses of Medicinal Plants and Natural Products. United States of America: IGI Global; 2020. p. 67-90. doi: 10.4018/978-1-7998-2094-9.ch004.
10. Sujith T, Susikumar S, Sunilkumar KN, Radha P, Shakila R, Gopinath P. Detection of adulteration of *Decalepis hamiltonii* Wight & Arn. with *Hemidesmus indicus* (L.) R. Br. by pharmacognostic, molecular DNA fingerprinting by RAPD, chemical and HPTLC studies. Plant Sci Today. 2021;8(3):610-20. doi: 10.14719/pst.2021.8.3.1151.
11. Mahalingam G, Kannabiran K. *Hemidesmus indicus* root extract ameliorates diabetes-mediated metabolic changes in rats. Int J Green Pharm. 2009;3(4):314-18. doi: 10.4103/0973-8258.59739.
12. Nandy S, Mukherjee A, Pandey DK, Ray P, Dey A. Indian sarsaparilla (*Hemidesmus indicus*): recent progress in research on ethnobotany, phytochemistry and pharmacology. J Ethnopharmacol. 2020;254:112609. doi: 10.1016/j.jep.2020.112609.
13. Sharma S, Shahzad A. An overview on *Decalepis*: a genus of woody medicinal climbers. J Plant Sci Res. 2014;1(1):104.
14. Susila AV, Sangeeta S. *Decalepis hamiltonii* (swallow root) as a potential antimicrobial agent against endodontic pathogens: an in vitro study. J Oper Dent Endod. 2021;6(1):1-5. doi: 10.5005/jp-journals-10047-0107.
15. Anonymous. A dictionary of Raw Materials. Wealth of India. CSIR, New Delhi, India; 1990. p. 1-161.
16. Sengupta M, Ghosh AK, Dalal I, Paul S. Anti-inflammatory activity of root of *Decalepis hamiltonii*. J Drug Deliv Ther. 2013;3(1):70-73. doi: 10.22270/jddt.v3i1.379.
17. Srivastava A, Shivanandappa T. Neuroprotective effect of *Decalepis hamiltonii* roots against ethanol-induced oxidative stress. Food Chem. 2010;119(2):626-9. doi: 10.1016/j.foodchem.2009.07.003.
18. Harvey AL, Edrada-Ebel R, Quinn RJ. The re-emergence of natural products for drug discovery in the genomics era. Nat Rev Drug Discov. 2015;14(2):111-29. doi: 10.1038/nrd4510.
19. Harish Nayaka MA, Sathisha UV, Dharmesh SM. Cytoprotective and antioxidant activity of free, conjugated and insoluble-bound phenolic acids from swallow root (*Decalepis hamiltonii*). Food Chem. 2010;119(4):1307-12. doi: 10.1016/j.foodchem.2009.08.044.
20. Sujith T, Murugammal S, Shakila R, Gopinath P. Screening and validated semi - quantification high-performance thin layer chromatography method development for lupeol, lupeol acetate, β-sitosterol, ρ-coumaric acid and proto-catechuic acid in the root extracts of *Hemidesmus indicus* (L.) R.Br. & *Decalepis hamiltonii* Wight & Arn. J Appl Res Med Aromat Plants. 2023;36:100510. doi: 10.1016/j.jarmap.2023.100510.
21. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the care and use of laboratory animals.

In: The National Academies Collection: Reports funded by National Institutes of Health. 8th ed. Washington, DC: National Academies Press (US); 2011. doi: 10.17226/12910.
22. Al-Saikhan FI, Ansari MN. Evaluation of the diuretic and urinary electrolyte effects of methanolic extract of *Peganum harmala* L. in Wistar albino rats. Saudi J Biol Sci. 2016;23(6):749-53. doi: 10.1016/j.sjbs.2016.01.025.
23. Shanmuganathan P, Kumarappan M. Evaluation of diuretic, saluretic and natriuretic activity of hydrochlorothiazide in combination with misoprostol in Wistar rats. Natl J Physiol Pharm Pharmacol. 2018;8(8):1226-9. doi: 10.5455/njppp.2018.8.0518731052018.
24. Gadge NB, Jalalpure SS. Natriuretic and saluretic effects of *Hemidesmus indicus* R. Br. root extracts in rats. Indian J Pharmacol. 2011;43(6):714-7. doi: 10.4103/0253-7613.89833.
25. Zanovello M, Bolda Mariano LN, Cechinel-Zanchett CC, Boeing T, Tazinaffo GC, da Silva LM, et al. *Tagetes erecta* L. flowers, a medicinal plant traditionally used to promote diuresis, induced diuretic and natriuretic effects in normotensive and hypertensive rats. J Ethnopharmacol. 2021;279:114393. doi: 10.1016/j.jep.2021.114393.
26. Solomon Raju AJ, Ramana KV. Traditional preparation of a health drink *Nannari Sharbat* from the root extract of *Decalepis hamiltonii* Wight & Arn. Indian J Nat Prod Resour. 2011;2(1):121-24.
27. Pullaiah CP, Kedam T, Nelson VK, Narasimha Kumar GV, Reddy DG. Supplementation of *Daucus carota* L. extract prevents urolithiasis in experimental rats. Indian J Nat Prod Resour. 2018;9(3):253-60.
28. Gamba G, Friedman PA. Thick ascending limb: the Na(+):K(+):2Cl (-) co-transporter, NKCC2, and the calcium-sensing receptor, CaSR. Pflugers Arch. 2009;458(1):61-76. doi: 10.1007/s00424-008-0607-1.
29. Graefe EU, Veit M. Urinary metabolites of flavonoids and hydroxycinnamic acids in humans after application of a crude extract from *Equisetum arvense*. Phytomedicine. 1999;6(4):239-46. doi: 10.1016/s0944-7113(99)80015-4.
30. Garg A, Garg S, Zaneveld LJ, Singla AK. Chemistry and pharmacology of the citrus bioflavonoid hesperidin. Phytother Res. 2001;15(8):655-69. doi: 10.1002/ptr.1074.
31. Kateel R, Rai MS, Ashok Kumar J. Evaluation of diuretic activity of gallic acid in normal rats. J Sci Innov Res. 2014;3(2):217-20. doi: 10.31254/jsir.2014.3216.
32. Zhang X, Li XY, Lin N, Zhao WL, Huang XQ, Chen Y, et al. Diuretic activity of compatible triterpene components of *Alismatis rhizoma*. Molecules. 2017;22(9):1459. doi: 10.3390/molecules22091459.
33. Srivastava A, Jagan Mohan Rao L, Shivanandappa T. Isolation of ellagic acid from the aqueous extract of the roots of *Decalepis hamiltonii*: antioxidant activity and cytoprotective effect. Food Chemistry. 2007;103(1):224-33. doi: 10.1016/j.foodchem.2006.08.010.
34. Ashalatha K, Venkateswarlu Y, Priya AM, Lalitha P, Krishnaveni M, Jayachandran S. Anti inflammatory potential of *Decalepis hamiltonii* (Wight and Arn) as evidenced by down regulation of pro inflammatory cytokines-TNF-alpha and IL-2. J Ethnopharmacol. 2010;130(1):167-70. doi: 10.1016/j.jep.2010.04.022.