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Impact of the Hydro-Ethanolic Extract of *Ficus umbellata* (Valh.) Leaves on Blood Pressure Regulation and Electrolyte Balance in Wistar Rats

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ABSTRAT :
The study aims to evaluate the hypotensive and ionic effects of the aqueous extract of Ficus umbellata on blood pressure and electrolyte balance in rats. Oral administration of the extract at doses of 100, 200, and 400 mg/kg for several days resulted in a significant, dose-dependent reduction in both systolic and diastolic blood pressure, particularly pronounced at 400 mg/kg. At the same time, notable changes in the blood ionogram were observed, including a decrease in sodium and chloride levels, accompanied by an increase in plasma potassium and calcium levels.
These effects suggest that Ficus umbellata exerts its antihypertensive action through several mechanisms, including peripheral vasodilation, a diuretic (natriuretic) effect, and modulation of ionic balance. The likely presence of flavonoids and phenolic compounds in the extract could explain these pharmacological effects. The results corroborate existing literature on the antihypertensive properties of certain medicinal plants.
This study thus supports the therapeutic potential of Ficus umbellata in the treatment of hypertension, while emphasizing the need for further studies to identify the active principles responsible and confirm its safety for human use.

Keywords: *Ficus umbellata, Hypotension, Blood Electrolytes, Diuretic Effect, Phytotherapy*

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I. INTRODUCTION

Hypertension (HTN) is one of the leading risk factors for cardiovascular diseases worldwide, contributing to over 10 million deaths each year according to the World Health Organization (WHO, 2021). It often results from a complex interaction between genetic, environmental, and metabolic factors, including imbalances in the metabolism of electrolytes such as sodium, potassium, and calcium, which directly influence blood pressure regulation via the kidneys and the autonomic nervous system (Carretero & Oparil, 2000; Touyz, 2004).

Despite the availability of several classes of antihypertensive medications, including angiotensin-converting enzyme (ACE) inhibitors, diuretics, calcium channel blockers, and beta-blockers, many patients experience undesirable side effects or partial resistance to treatment (Messerli et al., 2017). This has renewed interest in alternative therapeutic approaches, particularly phytotherapy, which involves the use of medicinal plants traditionally employed in African and Asian medicine (Ekor, 2014).

Among these plants, *Ficus umbellata* (Vahl) Miq., belonging to the Moraceae family, is widely used in African traditional medicine for treating various ailments, including hypertension, urinary infections, abdominal pain, and gynecological disorders (Akinmoladun et al., 2015). Preliminary phytochemical studies have revealed that the leaves of *Ficus umbellata* contain flavonoids, tannins, alkaloids, saponins, and other secondary metabolites with diverse pharmacological properties, including antioxidant, anti-inflammatory, and vasodilatory effects

(Yemele et al., 2011; Tédong et al., 2015). However, scientific data on the specific effects of this plant on blood pressure and ionic homeostasis remain limited.

In this context, the present study aims to evaluate the effects of *Ficus umbellata* leaf extracts on blood pressure and blood electrolyte balance in Wistar rats, an experimental model widely used in cardiovascular research. The goal is to provide experimental evidence to better understand the mechanisms by which this plant may exert antihypertensive effects and to assess its potential for the development of new natural therapeutic agents.

II. SETTING, MATERIALS AND METHODS

Setting

The experimental work was conducted at the Laboratory of Pharmacology and Improved Traditional Medicine (LPMTA) of the Faculty of Science and Technology (FAST) at the University of Abomey-Calavi (UAC), Republic of Benin. LPMTA is a multidisciplinary research laboratory recognized for its contributions to the pharmacological valorization of local medicinal plants, with the aim of developing effective and scientifically validated phytomedicines. The laboratory is equipped with the necessary infrastructure for in vivo experiments, pharmacological testing, and biochemical analyses, allowing for a rigorous evaluation of the biological effects of natural extracts.

Materials Used

Plant Material

The leaves of Ficus umbellata (Vahl) Miq. werecollected in February 2024 from the commune of Zè, located in the south of Benin. The botanical identification of the specieswascarried out at the National Herbarium of Benin (HNB) by Professor Monique TOSSOU and recordedunder the referencenumber YH870/HNB. After collection, the leaveswerecarefullywashedwith clean water to removeimpurities, thendried in the shade at room temperature for ten (10) days. Once fullydried, theyweregroundusing an electric grinder to obtain a homogeneous and fine powder, whichserved as the rawmaterial for the preparation of the extractused in the experiments.

Reagents and Solvents

The various reagents and solvents used in this study were of analytical grade (pro analysi) and were handled in accordance with good laboratory practices. These included:

- 70% Ethanol: Used for the preparation of the hydroethanolic extract of *Ficus umbellata* leaves (Sigma-Aldrich, USA).
- Sodium chloride (NaCl), potassium chloride (KCl), calcium chloride ($CaCl_2$), and magnesium chloride ($MgCl_2$): Used as standards or components of buffer solutions required for biochemical and electrolyte assays (Merck®, Germany).
- Sterile heparinized solution: Used for blood collection to prevent coagulation.
- Ketamine (Imalgène® 1000) and diazepam (Valium®): Used to induce anesthesia during biological sampling and dissection.
- Sterile distilled water: Used for all preparations, dilutions, and rinses to ensure the absence of ionic or microbial contamination.

Biological Material

The study was conducted on twenty-four (24) adult male Wistar rats, weighing between 180 and 220 g, obtained from the central animal facility of the Faculty of Science and Technology at the University of Abomey-Calavi (FAST/UAC). The animals were acclimatized for one week in polypropylene cages, with six rats per cage, in a room maintained at an ambient temperature of 22 ± 2 °C under a 12-hour light/dark cycle. They were fed standard pelleted rodent chow (Vitalac®) and had free access to drinking water ad libitum. Treatments were administered daily by oral gavage using flexible oral cannulas and 5 or 10 mL syringes, depending on the volume corresponding to the administered dose.

Methodology

Extraction

The extraction of bioactive compounds from *Ficus umbellata* leaves was carried out by maceration using a hydroethanolic solvent composed of 70% ethanol and 30% water. The plant powder was immersed in this solvent for 72 hours with intermittent agitation to enhance the extraction of active constituents. At the end of the maceration period, the mixture was filtered using filter paper to separate the solid residue from the filtrate containing the active principles. The resulting filtrate was then concentrated under reduced pressure using a rotary evaporator maintained at 40 °C, in order to remove the solvent while preserving thermosensitive compounds. The concentrate was subsequently dried in an oven at 45 °C until a homogeneous dry extract was obtained. Finally, the dry extract was stored in a tightly sealed container and kept at 4 °C in the dark until use in the experiments.

Study of the Efficacy of *Ficus umbellata* Extract on Cardiovascular Parameters and Ionic Balance

Experimental Conditions

The study involved 24 normotensive adult male Wistar rats, aged 8 to 10 weeks and weighing between 180 and 220 g. The animals were housed in polypropylene cages under controlled environmental conditions (temperature: 22–25 °C; relative humidity: 55–60%; light/dark cycle: 12 h). They were fed a standard diet and had free access to drinking water. A 7-day acclimatization period was observed prior to the start of the experiment.

Distribution of Experimental Groups

After a seven-dayacclimatizationperiod, the male Wistar rats used in the experimentwererandomlyassigned to four homogeneousexperimental groups, eachcomprising six (06) animals. This randomizationwascarried out whileconsidering initial body weights to ensurecomparabilitybetween groups and minimizeexperimentalbias.

- **Control group (T):** This group received only distilled water, administered orally at a dose of 10 mL/kg of body weight per day. It served as a baseline reference to assess physiological parameters without phytotherapeutic intervention.
- **FU100 group:** Animals in this group received a daily oral treatment with a hydroethanolic extract of *Ficus umbellata* leaves at a dose of 100 mg/kg body weight.
- **FU200 group:** Rats in this group were administered the same extract at an intermediate dose of 200 mg/kg/day via oral gavage.
- **FU400 group:** This group received the highest dose of the extract, 400 mg/kg/day, also by oral route.

The administration was conducted daily in a strictly controlled manner for fourteen (14) consecutive days to evaluate the dose-dependent impact of *Ficus umbellata* extract on cardiovascular and electrolyte parameters in rats.

Blood Pressure Measurement

Systolic (SBP) and diastolic blood pressure (DBP) were evaluated in all animals on days 0 (before treatment), 7, and 14 (during and after treatment) to monitor the progression of cardiovascular parameters under the influence of *Ficus umbellata* extract. Measurements were performed using a non-invasive tail-cuff system (CODA™, Kent Scientific, USA), based on the volumetric plethysmography technique.

This method, originally described by Bunag et al. (1973), involves restraining the rats in a suitable holder in a quiet environment with a controlled temperature (around 30 °C) to promote adequate blood flow to the tail. An inflatable cuff is placed at the base of the tail, and a pressure sensor detects volume changes in blood flow correlated with blood pressure.

For each rat, three consecutive measurements were taken during each session, after a familiarization period with the equipment to reduce stress and measurement artifacts. The arithmetic mean of the three readings was calculated and used as the representative SBP and DBP value for the animal at each time point.

Blood Collection and Electrolyte Assay

At the end of the treatment period (day 14), all animals were subjected to deep anesthesia via intraperitoneal injection of a ketamine (50 mg/kg) and diazepam (10 mg/kg) mixture, in accordance with ethical standards for laboratory animal handling. Once anesthesia was confirmed (absence of corneal reflex and response to painful stimulation), cardiac puncture was performed using a sterile syringe to collect blood into pre-heparinized tubes to prevent coagulation.

The collected blood was then centrifuged at 3000 rpm for 15 minutes at 4 °C to separate the plasma. The resulting plasma supernatant was carefully aspirated and stored at 4 °C for immediate analysis.

Plasma electrolyte levels, specifically sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-), were measured using a semi-automated electrolyte analyzer (Biolyte 2000 model, BioCare®). This device, based on ion-selective electrode (ISE) technology, enables rapid, accurate, and simultaneous determination of plasma ion concentrations, which is essential for evaluating hydro-electrolytic balance in the treated animals.

StatisticalAnalysis

Data wereexpressed as mean ± standard deviation (M ± SD). Comparisonsbetween groups wereperformedusing one-wayanalysis of variance (ANOVA), followed by Tukey's post hoc test. The significancelevelwas set at $p < 0.05$. Statisticalanalysiswascarried out usingGraphPadPrism version 8.0.

III. RESULTS

Effects of *Ficus umbellata*Extract on Blood Pressure

The results show a progressive and dose-dependent decrease in bothsystolic (SBP) and diastolic (DBP) blood pressure throughout the treatmentperiod.

Effects of *Ficus umbellata* Extract on Systolic Blood Pressure (SBP)

The analysis of the results (Table 1) reveals that the administration of the Ficus umbellata extract induces a progressive and significant decrease in systolic blood pressure (SBP) in Wistar rats in a dose-dependent manner. Indeed, SBP remained stable in the control group throughout the experiment, confirming the absence of spontaneous physiological fluctuations. In contrast, rats treated with 100 mg/kg of the extract exhibited a moderate but significant decrease in SBP by day 14 ($p < 0.05$). This reduction became more pronounced with the 200 mg/kg dose, with a significant decrease observed as early as day 7 ($p < 0.05$), which intensified by day 14 ($p < 0.01$). The hypotensive effect was maximal at the 400 mg/kg dose, with a highly significant reduction in SBP from the first week ($p < 0.01$), reaching 96.3 ± 2.5 mmHg on day 14. These data suggest that Ficus umbellata extract exhibits notable antihypertensive activity, likely due to vasodilatory, natriuretic effects, or modulation of neurohormonal systems involved in blood pressure regulation.

Table 1: Effects of *Ficus umbellata*Extract on Systolic Blood Pressure (SBP)

Group	SBP Day 0 (mmHg)	SBP Day 7 (mmHg)	SBP Day 14 (mmHg)
Control	119.5 ± 1.3	119.8 ± 2.1	119.2 ± 2.3
FU100	120.3 ± 2.2	114.4 ± 2.7	108.5 ± 2.6*
FU200	120.8 ± 1.4	111.2 ± 2.4*	102.7 ± 3.1**
FU400	121.1 ± 2.6	106.5 ± 2.2**	96.3 ± 2.5**

*$p < 0.05$; **$p < 0.01$ vs. control

Effects of *Ficus umbellata* Extract on Diastolic Blood Pressure

The evaluation of diastolic blood pressure (DBP) in Wistar rats also reveals a significant hypotensive effect of *Ficus umbellata* extract, following a pattern similar to that observed for systolic blood pressure. The control group shows stable DBP over the 14 days, confirming hemodynamic stability in untreated animals. In contrast, the groups receiving the extract exhibit a progressive and dose-dependent reduction in DBP. At the dose of 100 mg/kg, a moderate decrease is observed by day 7, followed by a significant reduction on day 14 (74.4 ± 1.9 mmHg; $p < 0.05$). At 200 mg/kg, the reduction becomes significant by day 7 (75.5 ± 2.1 mmHg; $p < 0.05$) and

intensifies on day 14 (69.3 ± 2.2 mmHg; $p < 0.01$). The effect is even more pronounced at the 400 mg/kg dose, with a significant drop in DBP by day 7 (72.1 ± 2.5 mmHg; $p < 0.01$), reaching 64.5 ± 2.0 mmHg on day 14 ($p < 0.01$). These results confirm the hypotensive activity of the extract on both systolic and diastolic components of blood pressure, suggesting a global action on cardiovascular regulation, possibly through mechanisms involving peripheral vasodilation, reduced vascular resistance, or neurohormonal modulation.

Table 2:Effects of *Ficus umbellata*Extract on Diastolic Blood Pressure (DBP)

Group	DBP Day 0 (mmHg)	DBP Day 7 (mmHg)	DBP Day 14 (mmHg)
Control	82.4 ± 2.5	81.9 ± 2.2	82.2 ± 2.3
FU100	83.2 ± 2.1	78.6 ± 2.0	74.4 ± 1.9*
FU200	83.0 ± 2.6	75.5 ± 2.1*	69.3 ± 2.2**
FU400	83.5 ± 2.3	72.1 ± 2.5**	64.5 ± 2.0**

*$p < 0.05$; **$p < 0.01$ vs. control

Effects of *Ficus umbellata* on Blood Ion Balance

At the end of the treatment (Day 14), the plasma analysis revealed that *Ficus umbellata* extract significantly modulated the concentrations of sodium, potassium, and calcium, especially at higher doses.

Plasma Electrolyte Concentrations

The analysis of the blood ionogram of Wistar rats treated with Ficus umbellata extract highlighted significant and dose-dependent changes in plasma concentrations of sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-) compared to the control group. In the control animals, the electrolyte values remained within physiological norms, indicating good ionic balance.

In the treated groups, a progressive decrease in sodium levels was observed depending on the dose administered: at 200 mg/kg, the natremia significantly decreased (138.5 ± 2.1 mmol/L; $p < 0.05$), while at 400 mg/kg, it dropped more sharply (136.2 ± 1.9 mmol/L; $p < 0.01$). This relative hyponatremia suggests a natriuretic effect of the extract, potentially contributing to the reduction in blood pressure through a decrease in extracellular volume.

In parallel, a progressive increase in potassium was noted, significant from FU200 ($p < 0.05$), and more pronounced at FU400 (5.1 ± 0.2 mmol/L; $p < 0.01$). This moderate hyperkalemia is beneficial from a cardiovascular perspective, as potassium promotes vascular relaxation and decreases myocardial excitability, reinforcing the hypotensive effect.

Plasma calcium also increased significantly starting from 200 mg/kg (2.6 ± 0.3 mmol/L; $p < 0.05$), reaching 2.9 ± 0.3 mmol/L at FU400 ($p < 0.01$). This increase may reflect either bone mobilization or enhanced intestinal absorption, with potential effects on vascular contractility and cellular signaling.

Finally, chloride significantly decreased with increasing doses, from 104.6 ± 2.1 mmol/L (control) to 99.4 ± 2.0 mmol/L at FU400 ($p < 0.01$). This hypochloremia, associated with the drop in sodium, suggests a combined action on renal tubular reabsorption.

Table 3:Effects of *Ficus umbellata* on Blood Ion Balance

Group	Na^+ (mmol/L)	K^+ (mmol/L)	Ca^{2+} (mmol/L)	Cl^- (mmol/L)
Control	142.3 ± 1.8	4.1 ± 0.3	2.1 ± 0.2	104.6 ± 2.1
FU100	140.8 ± 2.0	4.4 ± 0.2	2.3 ± 0.2	103.2 ± 1.9
FU200	138.5 ± 2.1*	4.7 ± 0.3*	2.6 ± 0.3*	101.5 ± 1.8*
FU400	136.2 ± 1.9**	5.1 ± 0.2**	2.9 ± 0.3**	99.4 ± 2.0**

*$p < 0.05$; ** $p < 0.01$ vs. Control

IV. DISCUSSION

The results of this study demonstrate that the extract of *Ficus umbellata* has a marked and dose-dependent hypotensive effect, observed on both systolic (SBP) and diastolic (DBP) blood pressure. These effects are accompanied by changes in plasma electrolyte concentrations, suggesting a complex mechanism involving the regulation of blood ion balance. These findings align with previous studies showing the pharmacological properties of certain medicinal plants in the management of hypertension. The analysis of the results shows a significant reduction in blood pressure in the groups treated with *Ficus umbellata* extract (FU), especially at doses of 200 mg/kg (FU200) and 400 mg/kg (FU400). Rats in the control group, which received no treatment, did not show any significant variations in blood pressure throughout the study, indicating stable pressure under normal conditions. In contrast, in the treated groups, both SBP and DBP decreased in a dose-dependent manner, with the effects being most pronounced in the FU400 group. These results corroborate previous studies reporting hypotensive effects of plant extracts, involving mechanisms such as vasodilation and inhibition of the renin-angiotensin system, which are well documented in the literature (Tawfik et al., 2012; Nwachukwu et al., 2015).

The observed hypotensive effect in the FU100, FU200, and FU400 groups is likely linked to peripheral vasomotor modulation, suggesting that *Ficus umbellata* extract may induce vasodilation, thus reducing vascular resistance. These results are consistent with those reported by Dehghani et al. (2016), who highlighted the hypotensive effects of certain plants rich in flavonoids and phenolic compounds, similar to those potentially present in *Ficus umbellata*.

The analysis of the blood ionogram reveals significant changes in the concentrations of sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-). *Ficus umbellata* extract induces a progressive decrease in plasma sodium starting at 200 mg/kg, with significantly lower levels at 400 mg/kg. This phenomenon is likely related to a natriuretic effect, which is well known for its contribution to lowering blood pressure. Sodium is a key ion in maintaining blood volume and regulating blood pressure. The reduction in sodium may suggest a diuretic effect, which promotes the elimination of sodium by the kidneys, thereby decreasing circulating volume and blood pressure (Bakker et al., 2004).

Concurrently, the elevation in plasma potassium observed in the treated groups (especially at 200 and 400 mg/kg) is another important aspect. Potassium plays a crucial role in vascular relaxation, cardiac contractility modulation, and blood pressure regulation (Mills et al., 2010). The increase in potassium may thus contribute to the hypotensive effect by promoting vasodilation and reducing peripheral vascular resistance. Furthermore, the increase in plasma calcium levels starting at 200 mg/kg and the hypochloremia observed at 400 mg/kg suggest interference with ion transport mechanisms at the cell membranes, possibly via an effect on ion channels or renal reabsorption of electrolytes. These electrolyte changes are typically associated with diuretic and hypotensive effects, as observed in other studies using plant extracts (Yao et al., 2014). The results suggest that the hypotensive effect of *Ficus umbellata* may be mediated by several mechanisms. First, peripheral vasodilation is induced by the flavonoids and phenolic compounds present in the extract, which may relax vascular smooth muscles, reducing peripheral vascular resistance and lowering blood pressure (Nwachukwu et al., 2015). Second, the extract appears to have a natriuretic and diuretic effect, increasing sodium excretion by the kidneys, thereby reducing blood volume and contributing to lower blood pressure (Bakker et al., 2004). Lastly, the increase in plasma potassium and calcium levels may have beneficial effects on vascular and cardiac function, further supporting the observed antihypertensive effect (Mills et al., 2010). These findings provide insight into the potential pharmacological use of *Ficus umbellata* in the management of hypertension and highlight its ability to influence key physiological processes such as vascular tone and electrolyte balance. Further research, including clinical trials, is needed to better understand the full therapeutic potential and safety profile of *Ficus umbellata* for hypertensive patients.

V. CONCLUSION

The study on the impact of *Ficus umbellata* extract on blood pressure regulation and electrolyte balance in Wistar rats highlights its potential as an antihypertensive agent. Oral administration of the hydro-ethanolic extract at various doses (100, 200, and 400 mg/kg) for 14 days resulted in significant reductions in both systolic and diastolic blood pressure, with the most pronounced effects seen at the higher doses. This decrease in blood pressure was accompanied by notable improvements in electrolyte balance, including more regulated levels of sodium, potassium, calcium, and chloride compared to the control group.

These findings suggest that *Ficus umbellata* extract may exert its effects through mechanisms such as vasodilation, diuresis, and modulation of ion channels. The results support the potential of this plant as a natural therapeutic approach for managing hypertension and electrolyte imbalances. However, further research is

necessary to fully elucidate the molecular mechanisms involved and to assess the long-term efficacy and safety of *Ficus umbellata* in the management of hypertension.

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