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

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ABSTRAT :
The studyaims to evaluate the hypotensive and ioniceffects of the aqueousextract 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 severaldaysresulted in a significant, dose-dependentreduction in systolic and diastolicblood pressure, particularlypronounced at 400 mg/kg. At the same time, notable changes in the bloodionogramwereobserved, including a decrease in sodium and chloridelevels, accompanied by an increase in plasma potassium and calcium levels.
TheseeffectssuggestthatFicus umbellataexertsits antihypertensive action throughseveralmechanisms, includingperipheralvasodilation, a diuretic (natriuretic) effect, and modulation of ionic balance. The likelypresence of flavonoids and phenolic compounds in the extractcouldexplainthesepharmacologicaleffects. The resultscorroborateexistingliterature on the antihypertensive properties of certain medicinal plants.
This studythus supports the therapeuticpotential of Ficus umbellata in the treatment of hypertension, whileemphasizing the need for furtherstudies to identify the active principlesresponsible and confirmitssafety for human use.

Keywords: *Ficus umbellata, Hypotension, Blood Electrolytes, DiureticEffect, Phytotherapy*

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I. INTRODUCTION

Hypertension (HTA) is one of the leadingriskfactors for cardiovasculardiseasesworldwide, contributing to over 10 million deathseachyearaccording to the World HealthOrganization (OMS, 2021). It oftenresultsfrom a complex interaction betweengenetic, environmental, and metabolicfactors, includingimbalances in the metabolism of electrolytessuch as sodium, potassium, and calcium, whichdirectly influence the regulation of blood pressure by the kidneys and the autonomicnervous system (Carretero&Oparil, 2000;Touyz, 2004).

Despite the availability of several classes of antihypertensive medications, includingangiotensin-converting enzyme inhibitors (ACE inhibitors), diuretics, calcium antagonists, and beta-blockers, many patients experienceundesirablesideeffects or partial resistance to treatment (Messerli et al., 2017). This situation has renewedinterest in alternative therapeuticapproaches, particularlyphytotherapy, which relies on the use of medicinal plants with a tradition of empirical use in African and Asian traditionalmedicine (Ekor, 2014).

Amongthese plants, *Ficus umbellata* (Vahl) Miq., belonging to the Moraceaefamily, iswidelyused in Africantraditionalmedicine for the treatment of variousailments, including hypertension, urinary infections, abdominal pain, and gynecologicaldisorders (Akinmoladun et al., 2015). Preliminary phytochemicalstudies have revealedthat the leaves of *Ficus umbellata*containflavonoids, tannins, alkaloids, saponins, and othersecondarymetaboliteswithvariedpharmacologicalproperties, includingantioxidant, anti-inflammatory, and

vasodilatoryeffects (Yemele et al., 2011;Tédong et al., 2015). However, scientific data on the specificeffects of this plant on blood pressure and ionichomeostasisremainlimited.

In thiscontext, the presentstudyaims to evaluate the effect of *Ficus umbellata*leafextracts on blood pressure and bloodelectrolyte balance in Wistar rats, an experimental model widelyrecognized for studyingcardiovascular pathologies. The goal is to provideexperimental data thatwill help betterunderstand the mechanismsthroughwhichthis plant couldexert an antihypertensive effect, and to assessitspotential for the development of new naturaltherapeutic agents.

II. SETTING, MATERIALS AND METHODS

Setting

The experimentalworkwascarried out at the Laboratory of Pharmacology and ImprovedTraditionalMedicine (LPMTA) of the Faculty of Science and Technology (FAST) at the University of Abomey-Calavi (UAC), in the Republic of Benin. The LPMTA is a multidisciplinaryresearchlaboratoryrecognized for its investigations into the pharmacologicalvalorization of local medicinal plants, with the aim of developing effective and scientificallyvalidatedphytomedicines. This laboratoryisequippedwith the necessary infrastructure for in vivo manipulations, pharmacologicaltesting, and biochemical analyses, enabling a rigorousevaluation of the biologicaleffects of naturalextracts.

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 variousreagents and solventsused in thisstudywere of analytical grade (pro analysi) and werehandledaccording to good laboratory practices. Theyinclude:
70% Ethanol**:**used for the preparation of the hydro-ethanolicextract of *Ficus umbellata*leaves (Sigma-Aldrich, USA).

- Sodium chloride (NaCl), potassium chloride (KCl), calcium chloride ($CaCl_2$), and magnesiumchloride ($MgCl_2$):used as standards or for buffer solutions necessary for biochemical and electrolyticassays (Merck®, Germany).
- Sterileheparinizedsolution:used for blood sampling to prevent coagulation.
- Ketamine (Imalgène® 1000) and diazepam (Valium®):used for anesthesia induction duringbiological sampling and dissection.
- Steriledistilledwater:used for all preparations, dilutions, and washes to ensure the absence of ionic or microbial contamination.

BiologicalMaterial

The studywasconducted on twenty-four (24) adult male Wistar rats, weighingbetween 180 and 220 g, obtainedfrom the central animal facility of the Faculty of Science and Technology at the University of Abomey-Calavi (FAST/UAC). The animalswereacclimatized for one weekin polypropylene cages, with six rats per cage, in a room maintained at ambient temperature (22 ± 2 °C) under a 12-hour light/dark cycle. Theywerefed standard pelleted rodent chow (Vitalac®) and had free access to drinking water ad libitum. Treatmentswereadministereddaily by oral gavage using flexible oral cannulas and 5 or 10 mL syringes depending on the dose to bedelivered.

Methodology

Extraction

The extraction of bioactive compounds from*Ficus umbellata*leaveswascarried out by macerationusing a hydroethanolic solvent composed of 70% ethanol and 30% water. The plant powderwasimmersed in this solvent for 72 hourswith intermittent agitation to enhance the extraction of active substances. At the end of the macerationperiod, the mixture wasfilteredusingfilterpaper to separate the solidresiduefrom the filtratecontaining

the active principles. The resultingfiltratewasthenconcentratedunderreduced pressure using a rotary evaporatormaintained at 40 °C, in order to remove the solvent whilepreservingthermosensitive compounds. The concentratewassubsequentlydried in an oven at 45 °C until a homogeneous dry extractwasobtained. Finally, the dry extractwasstored in a tightlysealed container and kept at 4 °C in the darkuntil use in the experiments.

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

Experimental Conditions

The studyinvolved 24 normotensiveadult male Wistar rats, aged 8 to 10 weeks and weighingbetween 180 and 220 g. The animalswerehoused in polypropylene cages undercontrolledenvironmental conditions (temperature: 22–25 °C; relative humidity: 55–60%; light/darkcycle: 12 h). Theywerefed a standard diet and had free access to drinking water. A 7-day acclimatizationperiodwasobservedprior 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 receivedonlydistilled water, administeredorally at a dose of 10 mL/kg of body weight per day. It served as a baselinereference to assessphysiologicalparameterswithoutphytotherapeutic intervention.
- **FU100 group:** Animals in this group received a daily oral treatmentwith a hydroethanolicextract of *Ficus umbellata*leaves at a dose of 100 mg/kg body weight.
- **FU200 group:** Rats in this group wereadministered the sameextract 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 wasconducteddaily in a strictlycontrolledmanner for fourteen (14) consecutivedays to evaluate the dose-dependent impact of *Ficus umbellata*extract on cardiovascular and electrolyteparameters in rats.

Blood Pressure Measurement

Systolic (SBP) and diastolicblood pressure (DBP) wereevaluated in all animals on days 0 (beforetreatment), 7, and 14 (during and aftertreatment) to monitor the progression of cardiovascularparametersunder the influence of *Ficus umbellata*extract. Measurementswereperformedusing a non-invasive tail-cuff system (CODA™, Kent Scientific, USA), based on the volumetricplethysmography technique.

This method, originallydescribed by Bunag et al. (1973), involvesrestraining the rats in a suitableholder in a quiet environmentwith a controlledtemperature (around 30 °C) to promoteadequateblood flow to the tail. An inflatablecuffisplaced at the base of the tail, and a pressure sensordetects volume changes in blood flow correlatedwithblood pressure.

For each rat, threeconsecutivemeasurementsweretakenduringeach session, after a familiarizationperiodwith the equipment to reduce stress and measurementartifacts. The arithmeticmean of the threereadingswascalculated 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 treatmentperiod (day 14), all animalsweresubjected to deepanesthesia via intraperitoneal injection of a ketamine (50 mg/kg) and diazepam (10 mg/kg) mixture, in accordance withethical standards for laboratory animal handling. Once anesthesiawasconfirmed (absence of corneal reflex and response to painful stimulation), cardiacpuncturewasperformedusing a sterile syringe to collectbloodintopre-heparinized tubes to prevent coagulation.

The collectedbloodwasthencentrifuged at 3000 rpm for 15 minutes at 4 °C to separate the plasma. The resulting plasma supernatantwascarefullyaspirated and stored at 4 °C for immediateanalysis.

Plasma electrolytelevels, specifically sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-), weremeasuredusing a semi-automatedelectrolyteanalyzer (Biolyte 2000 model, BioCare®). This device, based on ion-selectiveelectrode (ISE) technology, enables rapid, accurate, and simultaneousdetermination of plasma ion concentrations, whichis essential for evaluating hydro-electrolytic balance in the treatedanimals.

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. RESULT

Effects of *Ficus umbellata*Extract on Blood Pressure

The results show a progressive and dose-dependentdecrease 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) revealsthat administration of the *Ficus umbellata*extractinduces a progressive and significantdecrease in systolicblood pressure (SBP) in Wistar rats in a dose-dependentmanner. Indeed, SBP remained stable in the control group throughout the experiment, confirming the absence of spontaneousphysiological fluctuations. In contrast, rats treatedwith 100 mg/kg of the extractexhibited a moderate but significantdecrease in SBP by day 14 ($p< 0.05$). This reductionbecame more pronouncedwith the 200 mg/kg dose, with a significantdecreaseobserved as early as day 7 ($p< 0.05$), whichintensified by day 14 ($p< 0.01$). The hypotensive effectwas maximal at the 400 mg/kg dose, with a highlysignificantreduction in SBP from the first week ($p< 0.01$), reaching 96.3 ± 2.5 mmHg on day 14. These data suggestthat*Ficus umbellata*extractexhibits notable antihypertensive activity, likely due to vasodilatory, natriureticeffects, or modulation of neurohormonalsystemsinvolved 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 diastolicblood pressure (DBP) in Wistar rats alsoreveals a significant hypotensive effect of *Ficus umbellata*extract, following a pattern similar to thatobserved for systolicblood pressure. The control group shows stable DBP over the 14 days, confirminghemodynamicstability in untreatedanimals. In contrast, the groups receiving the extractexhibit a progressive and dose-dependentreduction in DBP. At the dose of 100 mg/kg, a moderatedecreaseisobserved by day 7, followed by a significantreduction on day 14 (74.4 ± 1.9 mmHg;$p< 0.05$). At 200 mg/kg, the reductionbecomessignificant 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 effectiseven 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 ($p< 0.01$). Theseresultsconfirm the hypotensive activity of the extract on bothsystolic and diastolic components of blood pressure, suggesting a global action on cardiovascularregulation, possiblythroughmechanismsinvolvingperipheralvasodilation, reducedvascularresistance, 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 analysisrevealedthat*Ficus umbellata*extractsignificantlymodulated the concentrations of sodium, potassium, and calcium, especially at higher doses.

Plasma Electrolyte Concentrations

The analysis of the bloodionogram of Wistar rats treatedwith*Ficus umbellata*extracthighlightedsignificant 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 remainedwithinphysiologicalnorms, indicating good ionic balance.

In the treated groups, a progressive decrease in sodium levelswasobserveddepending on the dose administered: at 200 mg/kg, the natremiasignificantlydecreased (138.5 ± 2.1 mmol/L; $p < 0.05$), while at 400 mg/kg, itdropped more sharply (136.2 ± 1.9 mmol/L; $p < 0.01$). This relative hyponatremiasuggests a natriureticeffect of the extract, potentiallycontributing to the reduction in blood pressure through a decrease in extracellular volume.

In parallel, a progressive increase in potassium wasnoted:significantfrom FU200 ($p < 0.05$), and more pronounced at FU400 (5.1 ± 0.2 mmol/L; $p < 0.01$). This moderatehyperkalemiaisbeneficialfrom a cardiovascular perspective, as potassium promotesvascular relaxation and decreasesmyocardialexcitability, reinforcing the hypotensive effect.

Plasma calcium alsoincreasedsignificantlystartingfrom 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 increasemayreflecteitherbonemobilization or enhanced intestinal absorption, withpotentialeffects on vascularcontractility and cellular signaling.

Finally, chloridessignificantlydecreasedwithincreasing doses, from 104.6 ± 2.1 mmol/L (control) to 99.4 ± 2.0 mmol/L at FU400 ($p < 0.01$). This hypochloremia, associatedwith the drop in sodium, suggests a combined action on renaltubularreabsorption.

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 thisstudydemonstratethat the extract of *Ficus umbellata* has a marked and dose-dependent hypotensive effect, observed on bothsystolic (PAS) and diastolic (PAD) blood pressure. Theseeffects are accompanied by changes in the plasma electrolyte concentrations, suggesting a complexmechanisminvolving the regulation of blood ion balance. Thesefindingsalignwithpreviousstudiesshowing the pharmacologicalproperties of certain medicinal plants in the management of hypertension.

The analysis of the results shows a significantreduction in blood pressure in the groups treatedwith*Ficus umbellata*extract (FU), especially at doses of 200 mg/kg (FU200) and 400 mg/kg (FU400). Rats in the control group, whichreceived no treatment, did not show anysignificant variations in blood pressure throughout the study, indicating stable pressure under normal conditions. In contrast, in the treated groups, both PAS and PAD decreased in a dose-dependentmanner, with the effectsbeingmostpronounced in the FU400 group. Theseresultscorroboratepreviousstudiesreporting hypotensive effects of plant extracts, involvingmechanismssuch as vasodilation and inhibition of the renin-angiotensin system, which are welldocumented in the literature (Tawfik et al., 2012;Nwachukwu et al., 2015).

The observed hypotensive effect in the FU100, FU200, and FU400 groups islikelylinked to peripheralvasomotor modulation, suggestingthat*Ficus umbellata*extractmayinducevasodilation, thusreducingvascularresistance. Theseresults are consistent withthosereportedby Dehghani et al. (2016), whohighlighted the hypotensive effects of certain plants rich in flavonoids and phenolic compounds, similar to thosepotentiallypresent in *Ficus umbellata*.

The analysis of the bloodionogramrevealssignificant changes in the concentrations of sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-). *Ficus umbellata*extractinduces a progressive decrease in plasma sodium starting at 200 mg/kg, withsignificantlylowerlevels at 400 mg/kg. This phenomenonislikelyrelated to a natriureticeffect, whichiswellknown for its contribution to loweringblood pressure. Sodium is a key ion in maintainingblood volume and regulatingblood pressure. The reduction in sodium maysuggest a diureticeffect, whichpromotes the elimination of sodium by the kidneys, therebydecreasingcirculating 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) isanother important aspect. Potassium plays a crucial role in vascular relaxation, cardiaccontractility modulation, and blood pressure regulation (Mills et al., 2010). The increase in potassium maythuscontribute to the hypotensive effect by promotingvasodilation and reducingperipheralvascularresistance.

Furthermore, the increase in plasma calcium levelsstarting at 200 mg/kg and the hypochloremiaobserved at 400 mg/kg suggestinterferencewith ion transport mechanisms at the cell membranes, possibly via an effect on ion channels or renalreabsorption of electrolytes. Theseelectrolyte changes are typicallyassociatedwithdiuretic and hypotensive effects, as observed in otherstudiesusing plant extracts (Yao et al., 2014).

The resultssuggestthat the hypotensive effect of *Ficus umbellata*maybemediated by severalmechanisms:The hypotensive effect of *Ficus umbellata*maybemediated by severalmechanisms. First, peripheralvasodilationisinduced by the flavonoids and phenolic compounds present in the extract, whichmay relax vascularsmooth muscles, reducingperipheralvascularresistance and loweringblood pressure (Nwachukwu et al., 2015). Second, the extractappears to have a natriuretic and diureticeffect, increasing sodium excretion by the kidneys, therebyreducingblood volume and contributing to lowerblood pressure (Bakker et al., 2004). Lastly, the increase in plasma potassium and calcium levelsmay have beneficialeffects on vascular and cardiacfunction, furthersupporting the observed antihypertensive effect (Mills et al., 2010).

Thesefindingsprovide insight into the potentialpharmacological use of *Ficus umbellata* in the management of hypertension and highlight itsability to influence key physiologicalprocessessuch as vasculartone and electrolyte balance. Furtherresearch, includingclinical trials, isneeded to betterunderstand the full therapeuticpotential 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 highlighted the antihypertensive and balancing potential of thismedicinal plant. Oral administration of the hydro-ethanolicextract at different doses (100, 200, and 400 mg/kg) for 14 daysresulted in a significantreduction in bothsystolic and diastolicblood pressure, particularlypronounced at higher doses. Simultaneously, a notable improvement in electrolytehomeostasiswasobserved, withbetter-regulatedlevels of sodium, potassium, calcium, and chloridecompared to the control group. Theseeffectssuggest a probable action of the extract on mechanisms of vasodilation, diuresis, and ion channel modulation. Thus, *Ficus umbellata*mayconstitute a promising source of bioactive compounds for the natural management of hypertension and associatedelectrolytedisorders. However, further investigations are needed to elucidate the molecularmechanismsinvolved and validateits long-termefficacy.

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