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Flavonoid profile of two antihypertensive extracts of *Trema orientalis* Blume leaves (Cannabaceae)

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ABSTRACT: In order to promote congolese plants with antihypertensive properties, two hypotensive (antihypertensive) extracts of *Trema orientalis* B. leaves were selected in order to know their flavonoid profiles. Therefore, these extracts were prepared and underwent bioguided fractionations until the isolation of the compounds on silica gel. These ethanolic and aqueous extracts presented similar characteristics (appearance, solubility in polar solvents, color of spots at UV 365 nm, frontal ratio). Five compounds were isolated from these extracts of *Trema orientalis* leaves. The analytical data of these compounds show a similarity of physical and chemical characteristics. These compounds presented in NMR^{1}H the same basic structure of the flavonoid type, 5,7,4'-trihydroxyl-2,3-dihydroflavonol (Kaempferol) or 5,7,4'-trihydroxyl-2,3-dihydroisoflavonol of gross formula $C_{15}H_{12}O_6$ and differ on their osidic part. Therefore, the definitive structural determination of these compounds must be confirmed by other more in-depth analyses. They will allow to valorize this plant by the production of phytoproducts rich in flavonoids antihypertensive and with oxidizing power.

KEYWORDS: flavonoid profile, trema orientalis, antihypertensive extracts, kaempferol, bioguided fractionation.

1 INTRODUCTON

Despite the damage caused by ¬harmful microorganisms, the ineffectiveness of some drugs currently available in the treatment of certain diseases makes it essential to search for new and more effective substances to combat all these diseases (cancer, diabetes, high blood pressure, AIDS, etc.) [1], [2], [3], [4], [5], [6].

To solve these problems, the modern pharmaceutical industry now relies on the diversity of metabolites from the plant world to find new molecules with novel biological properties [7], [8], [9], [10], [11], [12]. This source of metabolites seems inexhaustible since a small part of the known plant species have been studied on the phytochemical and biological levels, and each species can contain different bioactive or non-bioactive compounds [1], [13], [14]. These compounds are generally water-soluble such as alkaloids, polyphenols (especially flavonoids), terpenoids and steroids (especially saponins and cardiotonic heterosides) [11], [15], [16], [17]. Many studies suggest that polyphenols, especially flavonoids and tannins, are used as drugs to cure high blood pressure [18], [19], [20], [21].

In this context, isolating and identifying chemical substances with biological properties from plants is a major problem in phytochemistry and/or pharmacognosy. This requires means and techniques that sometimes allow obtaining the desired bioactive compounds [1], [22], [23].

To further enhance and identify substances with the biological properties of these plant species, we focused on the species *Tréma orientalis* Blume (Cannabaceae), a plant used by traditional health in Africa and Asia to treat a large number of pathologies [22], [23], [24], [25], [26], [27], [28], [29], [30].

In Africa in general and in Republic of Congo in particular, some work on extracts (alcoholic and aqueous) of the leaves of this plant has made it possible to evaluate their toxicity and proven the hypotensive (antihypertensive) effects on Wistar rats and vasorelaxant effects on the aortas of these rats [16], [19], [31], [32], [33], [34], [35], [36]. In addition, chemical studies carried out on *Tréma orientalis* B. have made it possible to identify several compounds without biological evaluation [12], [15], [19], [22], [23], [31]. It contains ((–) -epicatechin and (+) -catechin), xanthones and other molecules isolated and identified in its different parts [32], [37], [38], [39], [40].

The importance of polyphenols in medicine prompted us to know the phytochemical profiles of flavonoids present in the antihypertensive extracts of *Trema orientalis* B.

2 Materials And Methods

2.1 Preparation Of Plant Material

Trema orientalis B. leaves were collected in Brazzaville, Republic of Congo. Plant identification was made and recorded (specimen Sita, No. 445) at the National Herbarium of the Centre for Plant Resources Studies in Brazzaville. These leaves were dried in the shade at room temperature for three weeks and then ground to obtain a powder.

2.2 Preparation Of Extracts

The aqueous and alcoholic extracts are two hypotensive (antihypertensive) extracts of this plant, consumed by the Congolese population and pharmacologically validated, which were chosen and made the subject of this study. The aqueous extract was obtained after 5 % aqueous decoction of these leaves powder in 30 minutes. The alcoholic extract was obtained after successive exhaustion in Soxhlet of 100 g of powder of these leaves with 500 mL respectively of hexane, chloroform, ethyl acetate and ethanol [19], [23]. The significant mass of each extract was obtained by carrying out these operations several times.

2.3 Chemical Screening Of Polyphenols

The screening for metabolites of the extracts was done by Thin Layer Chromatography (TLC) using as support the aluminum plates in silica gel 60 F254 (Merck). The compounds such as flavonoids, phenolic acids and tannins were eluted and revealed using respectively the solvent system AcOEt/HCO_2H/H_2O (80/10/10 V/V/V) and the specific reagents Neu and $FeCl_3$ at 2 % for respectively flavonoids, phenolic acids, tannins and phenols. The observation of these compounds was made in the visible and UV 365 nm [19], [40].

2.4 Tests Of Carbonyl Groups Of Extracts

These tests were carried out by tube reactions according to the methods described in the literature. The developers used are $FeCl_3$, $AlCl_3$ and 2,4-dinitrophenylhydrazone (DNPH) reagents with or without heating [41], [42], [43].

2.5 Isolation Of Compounds On Open Column From Extracts

The extract was deposited on a silica gel column (Kieseigel 60 type) prepared in hexane. The elution was carried out respectively by a polarity gradient of the hexane/ethyl acetate system (100/00, 70/30, 50/50, 80/20, 00/100 V/V) followed by another ethyl acetate/ethanol mixture system (90/10, 80/20, 60/40 V/V) to obtain dry fractions after evaporation of the solvents. The last fraction obtained was fractionated again using successively the eluents petroleum ether/ethyl acetate (99/1, 0/100 V/V), ethyl acetate/methanol/formic acid (90/8/2, 85/11/4, 82/14/4, 80/15/5, 77/16/7, 60/40/00 V/V/V) and ethyl acetate/ethanol/water (95/10/5, 76/19/05 V/V/V) until obtaining subfractions each showing a single spot on TLC. These subfractions obtained were purified with the same elution system ethyl acetate/ethanol/water with polarities (85/10/5 V/V/V) and (77/17/6 V/V/V). The powder masses of the factions or compounds were obtained after evaporation of the solvents in a rotary evaporator at 40 °C. This operation was monitored on TLC at UV 365 nm after revelation of these compounds with Neu reagent [19], [23].

2.6 STRUCTURAL ANALYSIS OF ISOLATED COMPOUNDS

The proton nuclear magnetic resonance (^{1}HNMR) analyzes were carried out in deuterated dimethyl sulfoxide (DMSO). The NMR spectra of the compounds were obtained and recorded with the NMR devices of the Analysis Pole of Organic Compounds in Poitiers (France).

The processing of the spectra presented in this work was carried out using MesRenova program.

3 RESULTS ET DISCUSSION

Figure 1 shows the chromatographic profiles of the polyphenols of these two extracts of *Trema orientalis* leaves. The chromatographic profiles revealed with Neu and observed in UV 365 nm showed the presence of blue, green and yellow-orange fluorescence spots attributable to phenolic acids and flavonoids (Chromatogram A) [1], [23], [40].

However, we note a dominance of two spots of green and yellow-orange color (frontal ratios 0.29 and 0.38) in UV in the ethanolic and aqueous extracts. These spots observed in visible light take on a yellow and orange color respectively (Chromatogram B).

The revelation of these compounds with the 2 % $FeCl_3$ solution presented these spots with brown and violet colors in visible light at the same frontal ratios (Chromatogram C). These spots characterize the presence of tannins [1], [23].

Furthermore, the detection of carbonyl groups in these extracts was positive with $FeCl_3$, $AlCl_3$ and DNPH; which proves that these extracts contain compounds having this organic group in their structures. However, the presence of the carbonyl group could disqualify condensed tannins and validate the abundance of flavonoids in these extracts. The reaction of $FeCl_3$ on these polyphenols does not certify the presence of a carbonyl group in these compounds because this reagent also reacts with phenol [41], [42], [43].

These results confirm the work published in the literature by several authors who have shown the presence of flavonoids, phenolic acids and tannins in polar extracts obtained from the leaves of this plant in several countries of the world [40], [44], [45], [46], [47], [48], [49].

The biological properties of these polyphenolic compounds could justify the use of the leaves of this plant in traditional medicine to treat diseases such as high blood pressure, female sterility, malaria, cough, etc. [8], [15], [18], [44], [46], [50], [51].

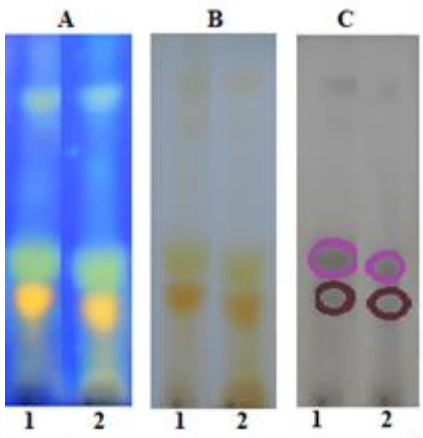

Fig. 1. Chromatographic profiles of polyphenols in extracts of these leaves

1: Ethanolic extract, 2: Aqueous extract, A: Developer: Neu, Observation: Visible;B: Developer Neu and observation of UV 365nm, C: Developer FeCl3 to 2% and Visible observation.

Fractionation of these two extracts of *Trema oriontalis leaves* allowed the isolation of 05 yellow solids including 04 solids noted compounds C1 to C4 with respective yields of 0.007 %; 0.003 %; 0.006 % and 0.005 % relative to 5 g of ethanolic extract and 01 solid noted compound C5 with a yield of 0.015 % relative to 2 g of aqueous extract (Figure 2). After revelation with Neu reagent and observation at UV 365 nm on TLC, these compounds each presented a single green or orange spot, with a frontal ratio of 0.38 in an solvent system (AcOEt/HCOOH/H_2O 80/10/10, V/V/V), which is characteristic of polyphenols, particularly

flavonoids. These results corroborate and confirm the work of Bonazaba et *al*. who identified spots of the same characteristics, on TLC at UV 365 nm, in the fractions from the ethanolic extract of leaves of the same congolese plant species [19], [23]. The presence of these compounds in this plant has also been confirmed by several works published in the literature [13], [17], [22], [52], [53], [54], [55]. These compounds being soluble in very polar solvents; which made it possible to consider the presence of very polar substituents such as osidic motifs in these compounds and to provide the additional information necessary for structural elucidation [1], [13], [40], [41], [56], [57], [58].

This solubility made it possible to carry out spectral analyses in deuterated DMSO to obtain usable ^{1}H NMR spectra (Figure 3).

Analysis of these proton spectra revealed that these compounds have a similarity of signals between 04.98 and 13.20 ppm; which allows us to say that they have an identical fragment of their basic structural. These compounds are differentiated by proton signals between 00.00 and 04.98 ppm; these are characteristic of the presence of other chemical groups or radicals associated with this basic fragment. These spectra show that these are polyphenols, in particular flavonoids, containing at least one carbohydrate in their structures [59].

The close similarities are observed between compounds 1 and 2 which exhibit 26 proton signals. However, they are differentiated in ^{1}H NMR by the presence and absence of a characteristic CH_3 peak (δ = 0.46 ppm) and two signals at 4.39 and 4.47 ppm respectively in these compounds.

Information on compounds 1, 2 and 5 allows one to consider the possibility of isomers or compounds with identical motifs.

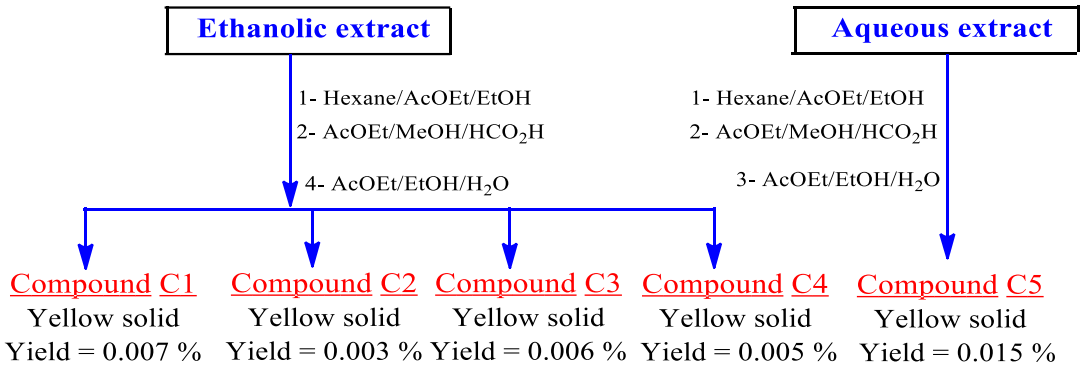

Fig. 2. Scheme of isolation of compounds from Trema oriontalis B leaves

Considering the similarity of the characteristics (appearance, color, frontal ratio, solubility, NMR and mass spectra) presented by these compounds isolated from these two extracts of the leaves of *Trema orientalis* B., some structural elements of these compounds are proposed from compound C1.

^{1}H NMR spectrum of compound 1 shows that this molecule has signals at δ = 6.26 (1H, sl), δ = 6.80 (1H, sl), δ = 6.90 (2H, d, *J* = 8.80 Hz) and δ = 8.04 (2H, d, *J* = 8.80 Hz) characteristic of the aromatic protons ($H_{8,}$ $H_{6,}$ $H_{3'}$ and $H_{2'}$) of the basic structure of flavonoids substituted in position 5 and 7 of his part A and in position 4' of his part B (Figures 4 and 5) [23], [59], [60], [61], [62], [63]. Two signals at δ = 10.38 (1H, s) and δ = 10.80 (1H, s) correspond respectively to the protons of the OH function *para*-substituted on the part B and substituted in position 5 on the part A of the flavonoids. Another signal resonating at δ = 13.15 (1H, s) is observed, this is characteristic of an OH function in position 7, in the vicinity of the carbonyl group of the basic ring of the flavonoids. These ^{1}H NMR data allow us to suppose that these five flavonoids have a basic structure of the 5,7,4'-trihydroxyl-2,3-dihydroflavonol (Kaempferol type) or 5,7,4'-trihydroxyl-2,3-dihydroisoflavonol. Furthermore, signals are observed at δ = 0.46 (3H, d, *J* = 6.10 Hz), between δ = 3.22 and δ = 3.57 (m), at δ = 4.32 (1H, sd, *J* = 5.20 Hz) and at δ = 5.26 (1H, sd, *J* = 4.70 Hz) which could be attributed to carbohydrate or sugar protons (Figures 4 and 6) [23], [63], [64].

The definitive structural determination of these compounds must be confirmed by further, more in-depth analyses.

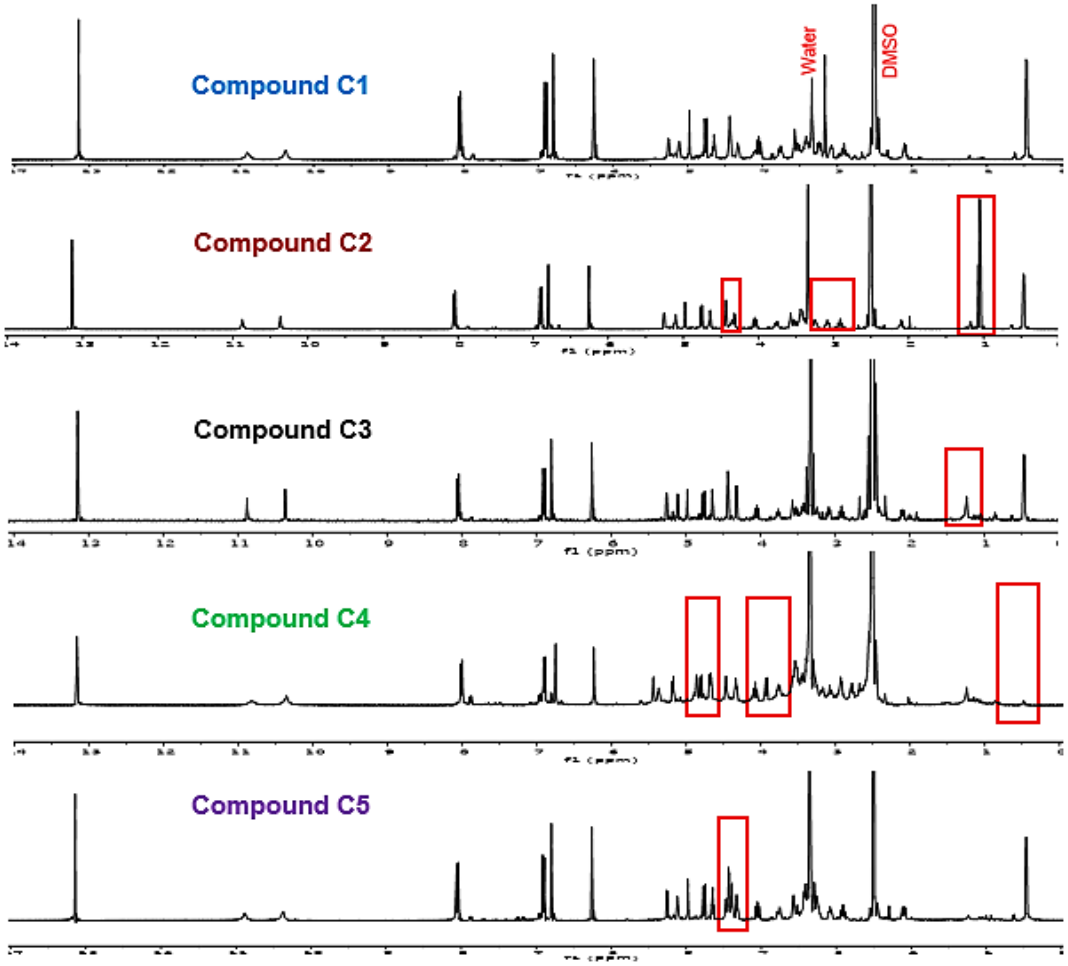

Fig. 3. *^{1}H NMR spectra of compounds isolated from Trema oriontalis B. leaves and carried out in deuterated DMSO*

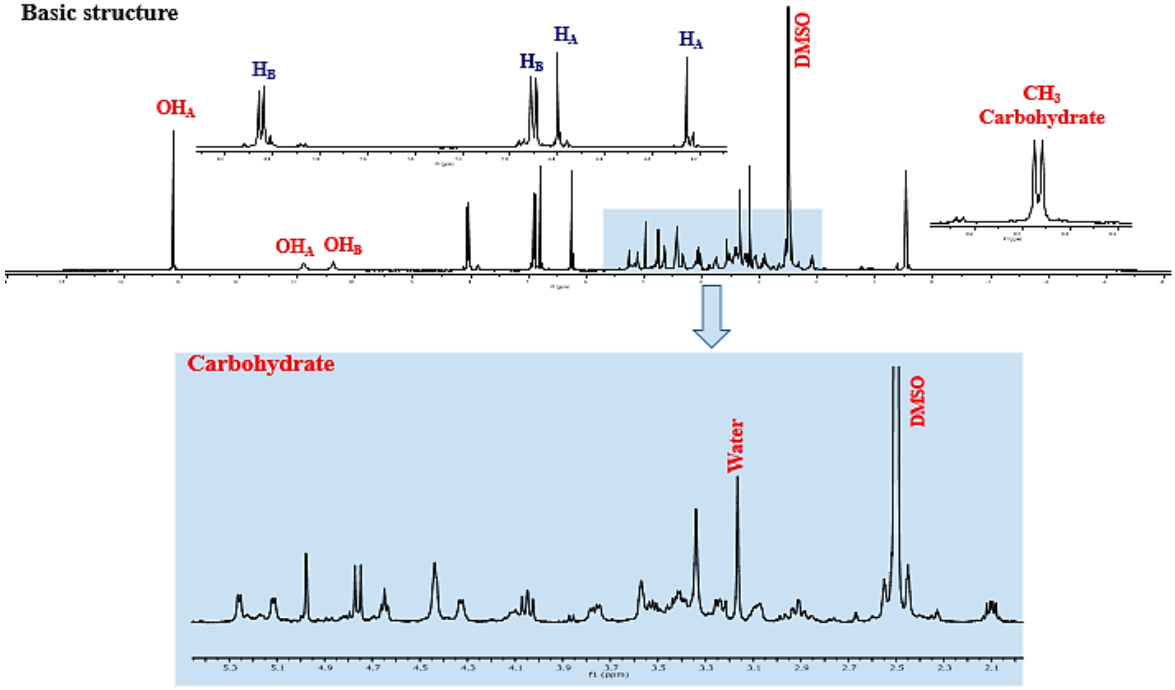

Fig. 4. *Detailed ^{1}H NMR spectra of compound C1 isolated of Trema oriontalis B. leaves and performed in deuterated DMSO*

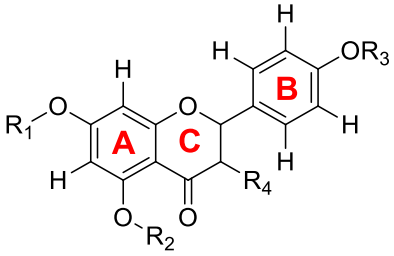

Fig. 5. Supposed basic structure of the compounds

R_1 at R_4 : H ou Carbohydrate

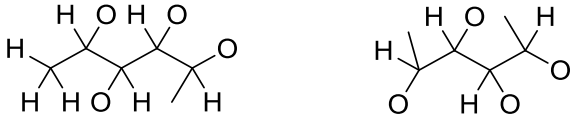

Fig. 6. Structural elements of carbohydrates identified in the isolated compounds

4 CONCLUSION

This work presents a phytochemical study to identify flavonoids from *Trema orientalis* leaves, an antihypertensive plant used in traditional congolese medicine. Among these compounds, five compounds were isolated from this plant. These compounds presented similar characteristics (appearance, solubility in polar solvents, color of spots at UV 365 nm, frontal ratio). The information on the proton spectra allowed to suppose the presence of a basic chemical structure of the type of substituted flavonoids (5,7,4'-trihydroxyl-2,3-dihydroflavonol) or 5,7,4'-trihydroxyl-2,3-dihydroisoflavonol) of at least one sugar in these compounds. This information requires in the future a definitive identification and confirmation of these flavonoids by other more in-depth analyses. They will allow to valorize this plant by the production of antihypertensive phytoproducts rich in flavonoids.

DECLARATION OF INTEREST

The authors declare that they have no conflict with any third party.

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REFERENCES

[1] Bruneton J., Pharmacognosie - Phytochimie, plantes médicinales. 4e éd. Revue et augmentée. Paris. Tec & Doc-Éd. Médicales internationales, 2009.
[2] Perrin, R. and Scharff, J.-P., *Chimie industrielle*. 2è édition, Masson Science, © Dunod, Paris, pp 159-165, 1999.
[3] C. Robitaille, S. Dai, C. Waters, L. Loukine, C. Bancej, S. Quach, J.Ellison, N. Campbell, K. Tu, K. Reimer, R. Walker, M. Smith, C. Blais and H. Quan, Diagnosed hypertension in Canada: Incidence, prevalence and associated mortality, *CMAJ*. Vol. 184, no. 1, pp. 49-56, 2012.
[4] Lhuillier A., Contribution à l'étude phytochimique de quatre plantes malgaches: Agauria salicifolia hook. f ex oliver, Agauria polyphylla Baker (ericaceae), Tambourissa trichophylla Baker (Monimiaceae) et Embelia concinna Baker (myrsinaceae), Thèse, Institut National Polytechnique de Toulouse, 2007.
[5] J. Lagarde Betti, J. Lejoly, Contribution to the knowledge of medicinal plants of the Dja Biosphere Reserve, Cameroon: Plants used for treating jaundice, *J. of Med. Plants Res.* Vol. 3, no. 12, pp. 1056-1065, 2009.
[6] M. S. Ali-Shtayeh, R. M. Jamous, R. M. Jamous and N. M. Y. Salameh, Complementary and alternative medicine (CAM) use among hypertensive patients in Palestine, *Complementary Therapies in Clinical Practice,* pp 1-8, 2013.

[7] F. Kunle Oluyemisi and H. O. Egharevba, Chemical constituents and biological activity of medicinal plants used for the management of sickle cell disease, *J. Med. Plants Resl*., Vol. 7, no 48, pp. 3452-3476, 2013.

[8] D. Niranjan, N. B. Shridhar, M. H. Vinuta, S. S. Manjunatha, U. Sunilchandra, B. S. Pradeep, G. U. Manju and R. P. Suresh, Botanical, pharmacological and toxicological properties of *Trema orientalis:* A Review, *The Journal of Phytopharmacology,* Vol. 12, no. 6, pp. 392-398, 2023.

[9] J. Dongsogo, C. Larbie, A. M. Idrissu, R. Appiah-Oppong, B. Emikpe and A. D. Abera, Medicinal Plants and Their Finished Marketed Herbal Products Used for Treatment of Liver Diseases in Ghana; A Field Survey and Review. *Res. J. Med. Plants,* Vol. 18, no. 1, pp. 13-23, 2024.

[10] E. Oppong Bekoe, C. Agyare, J. Sarkodie and D. Dadebo, Herbal Medicines Used in the Treatment of Typhoid in the Ga East Municipality of Ghana*. International Journal of Tropical Disease & Health,* Vol. 23, no 4, pp. 1-13, 2017.

[11] P. Anwar, A. K. Azad, Z. I. Muhammad, R. M. Mamunur, M. S. Sharif, R. Mizanur and A.K. Azad, A phytochemical and pharmacological review on *Trema orientalis*: a potential medicinal plant, *Newsletter, Vol.* 3, pp. 103-119, 2019.

[12] T. Napiroon, K. Tanruean, P. Poolprasert, M. Bacher, H. Balslev, M. Poopath and W. Santimaleeworagun, Cannabinoids from inflorescences fractions of *Trema orientalis* (L.) Blume (Cannabaceae) against human pathogenic bacteria, *PeerJ,* pp. 1-15, 2021.

[13] K. N'Guessan, G. N. Kadia, D. Zirihi, L. Taore, Ake-Assi Screening phytochimique de quelques plantes médicinales ivoiriennes utilisées en pays Krobou (Agboville, Côte-d'Ivoire), *Sciences &* Nature, Vol. 6, no. 1, pp. 1-15, 2009.

[14] A. Befinoana, J. S. Raso Amanan, A. Rakoto and G. Ralison, Sante orale et phytotherapie à madagascar, *Rev. d'odontost. Malg., Vol. 1,* pp. 42-50, 2010.

[15] M. Farzana, M. Mostazur Rahman, T. Ferdous and M. Sarwar Jahan, (2022) Review on *Trema orientalis* as a potential bioresource in tropical countries, *Trees, Vol.* 36, pp. 1169–1177, 2022.

[16] A. W. Etou Ossibi, R. D. G. Elion Itou, C. Nkounkou Loumpagou, J. D. Hibandza N., L. J. C. Bonazaba Milandou, J.-M Ouamba., A. A. Abena, Effets des extraits polaires des feuilles de *Trema orientalis* (Linn.) Blume (Ulmaceae) sur la pression artérielle moyenne chez le rat, *Revue CAMES – Série Pharm. Méd. Trad. Afr*., Vol. 18, no. 1, pp. 8-15, 2016.

[17] C. Nkounkou Loumpangou, A. W. Etou Ossibi, L. J. C. Bonazaba Milandou, B. I. Tsati Koussoukama, P. U. Bazolo Mampouya, J.-M. Ouamba, A. A. Abena, Caractérisation Phytochimique et Toxicité aigüe des feuilles de *Trema orientalis* (L.) Blume (Cannabaceae), *J. Soc. Ouest-Afr. Chim., Vol. 042*: 52- 59, 2016.

[18] S. A. Al-Robai, S.A. Zabin, A. A. Ahmed, H. A. Mohamed, A. A. A. Alghamdi, A. A. E. Ahmed, Phenolic contents, anticancer, antioxidant, and antimicrobial capacities of MeOH extract from the aerial parts of *Trema orientalis* plant, *Open Chemistry, Vol.* 20, pp. 666–678, 2022.

[19] L. J.C. Bonazaba Milandou, C. Nkounkou Loumpangou, H. Carreyre, J. Bescond, C. Vandebrouck, A. W. Etou Ossibi, J.-M. Moutsambote, J.-M. Ouamba, S. Thibaudeau and A. A. Abena, Bio-guided fractionation of the ethanolic extract from leaves of *Trema orientalis* Blume (Cannabaceae), a presumed antihypertensive plant from Congo-Brazzaville, *European Journal of Medicinal plants,* Vol. 20, no. 4, pp. 1-14, 2019.

[20] R. J. Jegede, J. E. Olajide and O. J. Ogunbiyi, Diuretic potential of he 50% ethanol-methanol extract of *Trema Orientalis* leaves in albino rats, *International Journal of Pharmaceutical Research and Applications,* Vol. 6, no. 5, pp. 84-92, 2021.

[21] B. B. Boua, J. Mamyrbekova-Bekro, B. A. Kouamé, Y. A. Bekro. Études chimique et pharmacologique de deux plantes utilisées dans le traitement traditionnel de l'hypertension artérielle à Assoumoukro (Côte d'ivoire*). Eur. J. of Scien. Res*., Vol. 97, no. 3, pp. 448-462, 2013.

[22] A. Dinortey, B. Michael, I. K. Galyuon, A. N. Oteng, *Trema orientalis* Linn. Blume: A potential for prospecting for drugs for various uses, *Pharmacogn Rev.,* Vol. 7, no. 13, pp. 67-72, 2013.

[23] Bonazaba Milandou L. J. C., Fractionnement et caractérisation des extraits de Trema orientalis Blume (Cannabaceae), une plante présumée antihypertensive au Congo-Brazzaville vers la valorisation en milieu superacide, Thèse de Doctorat, Université Marien Ngouabi, 2017.

[24] E. B. Wijaya, L. Riniwasih, Antibacterial activity test of *Trema orientalis l. Blumae* (anggrung) granule extract against bacteria salmonella sp. With the wet granulation method, *Indonesia Natural Research Pharmaceutical Journal,* Vol. 5, no. 1, pp. 45-53, 2020.

[25] P. O. Fabowale, A. O. Ogundare, P. Awoyinka and O. Agunloye, *Trema orientalis* Linn. Blume: Susceptibility Patterns of Selected Multiple Antibiotic Resistant Bacteria and Fungi to the Leaf Extracts, *South Asian Journal of Research in Microbiology,* Vol. 8, no. 2, pp. 25-32, 2020.

[26] A. A Rafatou Adjileye, A. M. O Amoussa, R. Adamou, B. Awede, A. Sanni, A. Laleye, L. Lagnika, Antihypertensive effect of *Dialium guineense* Wild. and *Trema orientalis* L. in L-NAME-induced hypertensive rats, *The Journal of Phytopharmacology,* Vol. 9, no. 1, pp. 5-11, 2020.

[27] K. Tokou Labite, K. Togbenou, K. Dosseh, K. Idoh, T. Kpatcha, A. Agbonon, Diuretic effects and subacute toxicity of *Trema orientalis* Linn leave extract in wistar rats, *Journal of Drug Delivery and Therapeutics,* Vol. 13, no. 4, pp. 46-53, 2023.

[28] M. Kabir, A. AL-Noman, B. Kumar Dash, M. Hasan, S. Akhter, M. Rahman, *Trema orientalis* (Linn.) leaves promotes anticancer activity in Ehrlich ascites carcinoma (EAC) in Swiss albino mice. DE GRUYTER, *Journal of Basic and Clinical Physiology and Pharmacology, no.* 20190121, pp. 1-12, 2019.

[29] G. Ajayi, A. Idoko, A. Usman, phytochemical analysis and antibacterial activity of *Trema orientalis* (Ulmaceae) stem bark extracts on respiratory tract bacteria, *Trop J Nat Prod Res,* Vol. 2, no. 12, pp. 512-516, 2019.

[30] K. N. Jiji, C. Pramod, S. P. Boby, D. R. P. Muralidharan, Evaluation of antidiabetic activity of ethanolic extract of *Trema orientalis* (L.) Blume leaves, *IOSR Journal of Pharmacy and Biological Sciences,* Vol. 11, no. 5, pp. 17-26, 2016.

[31] Pamisha P., Antiplamodial Neolignans from Trema Orientalis - Identification, Synthesis and Analogue Génération, Thèse, Université de Cape Town, 2012.

[32] T. Dimo, F. T. Ngueguim, P. Kamtchouing, E. Dongo, P. V. Tan, (2006). Glucose lowering efficacy of the aqueous stem bark extract of *Trema orientalis* (Linn) Blume in normal and streptozotocin diabetic rats, University of Yaounde I, *Pharmazie,* no. 61, pp. 233–236.

[33] S. K. Jain and S. Sumita, Traditionnal use of someIndian plants amongislanders of the Indian Ocean, *Indian J. Tradit. l Knowledge,* Vol. *4,* no. 4, pp. 345-357, 2005.

[34] K. Tuo, S. Béourou, A. Touré, Offianan, K. Ouattara, S. Meité, A. B. Ako Ako, S. S. Yao, D. Koffi, B. Coulibay, A. Coulibaly, A. J. Djaman, Antioxidant activities and estimation of the phenols and flavonoids content in the extracts of medicinal plants used to treat malaria in Ivory Coast. *Int. J. Curr. Microbiol. App.Sci*., Vol. *4,* no. 1, pp. 862-874, 2015.

[35] R. AA Adjileye, A. M. O. Amoussa and L. Lagnika, *Trema orientalis* L. and *Dialium guineense* Wild. used to manage hypertension in Bénin: phytochemical study and antioxidant activity, *Journal of Medicinal Plants Studies,* Vol. 7, no. 3, pp. 43-48, 2019.

[36] T. Hemalatha, D. Ahino Mary, A. Saravana Ganthi, Acute and sub-acute toxicity study of *Trema orientalis* (L.) Bl. Methanol extract in rats, *Journal of Drug Delivery and Therapeutics,* 2019; Vol. 9, no. 1-s, pp. 307-311, 2019.

[37] A. Mekarunothai, M. Bacher, R. Buathong, S. Intarasam, N. Tayana, S. Kongkiatpaiboon, T. Charoenrat and T. Napiroon, β-sitosterol isolated from the leaves of *Trema orientalis* (Cannabaceae) promotes viability and proliferation of BF-2 cells, *PeerJ,* no. 12: e16774, pp. 1-15, 2024.

[38] R. Das, S. Agrawal, P.Kumar, A. K. Singh, P. K. Shukla, I. Bhattacharya, K. N. Tiwari, S. K. Mishra, A. K. Tripathi, Network pharmacology of apigenilavan: a novel bioactive compound of *Trema orientalis* Linn. in the treatment of pancreatic cancer through bioinformatics approaches. *Biotech.,* Vol. 13, no. 160, pp. 1-20, 2023.

[39] A. Saleh, S. M. Zainal-Ariffin, S. F. Yahaya, A. G. Khaleel, Antioxidant activities and estimation of phenol and flavonoid contents in the extracts of *Trema orientalis* Linn Blume, *Nigerian Veterinary Journal,* Vol. 41, no. 2, pp. 73-84, 2020.

[40] Wagner H. and Bladt S., *Plant drug analysis a thin layer chromatography,* Atlas. 2nd édition, Berlin: Springer-Verlag, 1996.

[41] Z. Samira, C. Lorraine, R. Mohammad Abd El, K. Ali, Iyad K., Acétalisation verte du glycérol et du carbonyle catalysée par $FeCl_3.6H_2O$, *Catalyse moléculaire,* no. 438, pp. 204-2013, 2017.

[42] MyMaxicours, *Oxydation d'un alcool et d'un aldéhyde,* 2024.
[Online] Available: https://www.maxicours.com/se/cours/oxydation-d-un-alcool-et-d-un-aldehyde/ (Octobre 04, 2024).

[43] R. Corriu, M. Doré, R. Thomassin, Mécanisme de la C-acylation: Étude cinétique du mécanisme de la benzoylation des composés aromatiques catalysés par $AlCl_3$, *Tétraèdre,* Vol. 27, no. 22, pp. 5601-5618, 1971.

[44] I. T. Gbadamosi, J. O. Moody, A. O. Yekini, Nutritional Composition of Ten Ethnobotanicals Used for the Treatment of Anemia in Southwest Nigeria. *Eur. J. of Med. Plants.* Vol. 2, no. 2, pp. 140-150, 2012.

[45] M. Farzana, M. Mostazur Rahman, T. Ferdous and M. Sarwar Jahan, Review on *Trema orientalis* as a potential bioresource in tropical countries, *Trees,* Vol. 36, pp. 1169–1177, 2022.

[46] K. Tokou Labite, K. Togbenou, K. Dosseh, K. Idoh, T. Kpatcha, A. Agbonon, Diuretic effects and subacute toxicity of *Trema orientalis* Linn leave extract in wistar rats, *Journal of Drug Delivery and Therapeutics,* Vo. 13, no. 4, pp. 46-53, 2023.

[47] A. Saleh, S. M. Zainal-Ariffin, S.F. Yahaya, A.G. Khaleel, Antioxidant activities and estimation of phenol and flavonoid contents in the extracts of *Trema Orientalis* Linn Blume, *Nigerian Veterinary Journal,* Vol. 41, no. 2, pp. 73-84, 2020.

[48] V. G. Kanase and J. Singh. Evaluation of antipyretic and antiulcer activity of ethanolic extract of leaves of *Trema orientalis* L. in albino wistar rats, *Asian J Pharm Clin Res,* Vol. 12, no.12, pp. 149-154 2019.

[49] P. O. Fabowale, O. Agunloye and I. C. Adekanmbi. Comparative Screening of Phytochemicals and Bioactive Compounds of *Trema orientalis* (Linn. Blume) leaf and bark extracts, *Asian Journal of Research in Biochemistry,* Vol. 13, no. 2, pp. 7-16, 2023.

[50] C. Pramod, M. Ratheesh, P. J. Svenia and J. Stephy, Evaluation of hypolipidemic activity of ethanolic extract of *Trema orientalis* L. Blume leaves, *Journal of Pharmacognosy and Phytochemistry,* Vol. 9, no. 4, pp. 904-911, 2020.

[51] J. E. Olajide, M. Sanni, O. J. Achimugu, M. S. Suleiman, E. R. Jegede, V. D. Sheneni, Effect of methanol extract of *Trema orientalis* leaf on some biochemical and histopathological indices of wistar albino rats with cadmium-induced-hepatotoxicity, *Scientific African,* Vol. 10, no. e00568, pp. 1-9, 2020.

[52] W.-L. Kuo, H. Yu-Ling, W. Shr-Ting, N. Ching-Li, S. Bor-Jinn, C. Chien-Chih, Chemical constituents of *Trema orientalis, J. Chin. Med.,* Vol. 18, no. 1,2, pp. 27-36, 2007.
[53] A.G. Khaleel, Antioxidant activities and estimation of phenol and flavonoid contents in the extracts of *Trema orientalis* Linn B., *Nigerian Veterinary Journal,* Vol. 41, no 2, pp. 73-84, 2020.
[54] I. Idrus, J. Mukaddas, F. Mustafa. Isolasi dan identifikasi flavonoid ekstrak daun anggrung (*Trema orientalis* bi) secara spektrofotometri infra. Yayasan akrab pekanbaru, *Jurnal Akrab Juara,* Vol. 5, no. 4, pp. 177-184, 2020.
[55] L. Lachat, Caractérisation des composés phénolique présents dans deux espèces du genre Alchemilla, Filière technologie du vivant, Diplôme: Hes.so//HES-SO Valais, pp. 1-34, 2001.
[56] D. E. Giannasin, Generic relationships in the ulmaceae based on flavonoid chemistry, *Taxon,* Vol. 27, no. 4, pp. 331-344, 1978.
[57] M. R. Patel and H. S. Pancha. Isolation and Identification of Flavonoid Compounds in *Trema orientalis* Leaves by Preparative TLC and Various Spectroscopic Techniques, *Int J Ayu Pharm Chem,* Vol. 6, no. 1, pp. 238-244, 2017.
[58] Haidara M.A., Etude de la phytochimie et de l'activité anti-hypertensive de trois (3) plantes et d'une recette utilisées dans le traitement traditionnel de l'hypertension artérielle, Thèse, Université de Bamako, 2008.
[59] N. Fabre, I. Rustan, de H. Edmond and J. Quetin-Leclercq, Determination of flavone, flavonol, and flavanone aglycones by negative ion liquid chromatography electrospray ion trap mass spectrometry, *J Am Soc Mass Spectrom,* no. 12, pp. 707-715, 2001.
[60] Portet B., Recherche bioguidée de molécules antipaludiques d'une plante guyanaise, Piper hostmannianum Var. berbicense, Thèse, Université Paul Sabatier Toulouse III, 2007.
[61] Bi Koffi Kouame F.-P., *Valorisation de quatre plantes médicinales ivoiriennes: étude phytochimique,* Thèse, Université De Nantes et de L'Université De Cocody-Abidjan, 2012.
[62] Boutaghane N., Etude phytochimique et pharmacologique de plantes médicinales Algériennes Genista ulicina Spach (Fabaceae) et Chrysanthemum macrocarpum (Sch. Bip.) Coss. & Kralik ex Batt (Asteraceae), Thèse, Université de Constantine 1, 2013.
[63] Harkati B., Valorisation et identification structurale des principes actifs de la plante de la famille asteraceae: Scorzonera Undulata, Thèse, Université Mentouri- Constantine, 2011.
[64] Coulerie P., Étude phytochimique et pharmacologique de plantes de Nouvelle-Calédonie à potentialités anti-dengue, Thèse, Université de la Nouvelle-Calédonie, 2012.