Available Online at http://www.journalajst.com

ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

ISSN: 0976-3376

Asian Journal of Science and Technology
Vol. 13, Issue, 09, pp.12193-12198, September, 2022

RESEARCHARTICLE

PHENOLICS COMPOUNDS ISOLATED FROM *XIMENIA AMERICANA* L. (OLACACEAE) TRUNK BARK USED IN THE TRADITIONAL TREATMENT OF HYPERTENSION

ZAKARI SEYBOU Djamilatou[1, 2,*], VIRIEUX David[2], PIRAT Jean Luc[2] and SABO HaouaSeini

[1]Laboratoire des substances naturelles et de synthèse Organique (LASNASO), Université Abdou Moumouni de Niamey, Niger; [2]Laboratoire AM2N, Institut Charles Gerhardt, UMR 5253, Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM), 8, rue de l'Ecole Normale, 34296 Montpellier, France

ARTICLE INFO

Article History:
Received 25th June, 2022
Received in revised form
19th July, 2022
Accepted 14th August, 2022
Published online 30th September, 2022

Keywords:
X. Americana, Pyrogallol, Catechol, Protocatechuic Acid, Epicatechin, Hypertension

ABSTRACT

Ximenia americana L. (*X. americana*) is a medicinal shrub used in Niger and West Africa for the treatment of various diseases, the most common of which are infectious, inflammatory, and viral diseases. Particularly in Niger, the trunk bark of this plant is use in the traditional treatment of hypertension.Our study aims to identify phenolic compounds with antihypertensive or antioxidant properties of extracts of the trunk bark of this plant by extraction, then fractionation with solvents of increasing polarity (respectively hexane, chloroform, ethyl acetate and n-butanol) and purification by chromatography (normal open column and TLC). The resonance magnetic nuclear (RMN) analyses 1D (^{1}H AND ^{13}C) and 2D (HMQC, HMBC, DEPT) allowed to determine the structure of pyrogallol (compound1), protocatechuic acid (compound 2), catechol (compound 3) and epicatechin (compound 4). These novel compounds of *X. americana* L. bark were isolated for the first time.The presence of these compounds in this plant could justify its use in the traditional management of hypertension.

Citation: ***ZAKARI SEYBOU Djamilatou, VIRIEUX David, PIRAT Jean Luc and SABO HaouaSeini*, 2022.**"Phenolics compounds isolated from ximeniaamericana L. (olacaceae) trunk bark used in the traditional treatment of hypertension.",*Asian Journal of Science and Technology*, 11, (09), 12193-12198.

INTRODUCTION

High blood pressure, also known as the "silent killer", is a real public health problem. It is the major risk factor for cardiovascular disease. The increasing prevalence of this condition precedes the trend towards a global epidemic of unhealthy ageing. The World Health Organization (WHO) estimates that the cost of not committing to and investing in the prevention and treatment of cardiovascular disease could be as high as $47 billion worldwide over the next 25 years (Andrea and Eric, 2015). The consequences will be most severe in developing countries, as 80% of cardiovascular disease deaths occur in low and middle-income countries. In Niger its prevalence is 21.2% (MSP, 2008).However, the management of hypertension is a lifelong treatment and remains costly despite the therapeutic advances made with conventional drugs. As the income of the majority of the population is too low to be treated with conventional medicine, they resort to traditional medicine which is perceived as a primary means of health care in Niger (Aissa et *al*., 2017). It is therefore necessary to put in place preventive strategies and comprehensive management of hypertension that can be used by everyone.

Correspondingauthor: [1,2]*ZAKARI SEYBOU Djamilatou
[1]Laboratoire des substances naturelles et de synthèse Organique (LASNASO), Université Abdou Moumouni de Niamey, Niger; [2]Laboratoire AM2N, Institut Charles Gerhardt, UMR 5253, Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM), 8, rue de l'Ecole Normale, 34296 Montpellier, France.

In recent years, numerous studies have demonstrated the benefits of polyphenols on human health (Yousepan et *al*; 2018), and particular attention has been paid to their beneficial effect on hypertension (Jimenez et al et *al*., 2007, Helmut et *al*.,2016, Moreno-Luna et *al*., 2012), and cardiovascular disease(Jimenez et al et *al*., 2007, Helmut et *al*.,2016, Galleano et *al*., 2010). New sources of polyphenols are being sought. These are natural compounds that are widely distributed in the plant kingdom and are becoming increasingly important due to their role as antioxidants (Yousepan et *al*; 2018, Baudin, 2020).It is in this perspective that following an ethnobotanical survey on plants used in the management of hypertension in Niamey, we chose to characterise the phenolic compounds of the trunk bark *X. Americana* L. To our knowledge, there is no research to date on the characterization of phenolic compounds from extracts of this plant. The present study aims to extract, isolate and determine the structure of phenolic compounds with anti-hypertensive or antioxidant properties from the bark of this plant.

EXPERIMENTAL

Plant Material:The plant material is composed of the trunk bark of *X. americana* collected in June 2018 in Tara (Gaya). It was identified at the Biology Department of Abdou Moumouni University of Niamey by Professor Sadou MAMANE. The sample was dried under permanent ventilation for two weeks and then pulverised using an electric grinder (Brand RETSCH, Type SK 100) and preserved at lab temperature until use.

Figure1. Leaves, fruits and stem bark of *X. americana*

Extraction and fractionation: 500g of plant powder was macerated in 1.5L of methanol for 24 h under permanent stirring. After filtration, the resulting macerate was concentrated to dryness under reduced pressure at 40°C using a rotary evaporator. The methanol dry extract obtained was suspended in 300 ml of water and then extracted successively with hexane (5 x 300 ml), chloroform 5 x 300 ml, ethylacetate (5 x 300 ml) and n-butanol (5 x 300 ml). The solvents were removed under vacuum, the resulting hexane (2.5g); $CHCl_3$ (1.25g); EtOAc (8.86g), BuOH (95g) extracts were stored in sealed vials at laboratory room temperature (N'Guessan et *al*., 2011Le et *al*., 2012).

Isolation and purification: The EtOAc extract (3.5g) was chromatographed on a normal open column, using 120g of 40-63µm silica. Elution was carried out with a gradient of a mixture of three solvents CH_2Cl_2/AcOEt/MeOH. The ratio of CH_2Cl_2/AcOEt was set at 8:2, the polarity gradually increased with methanol. The collected fractions were analysed by TLC to determine those with a similar chromatographic profile at wavelengths of 254nm and 365nm and then revealed with phosphomolybdic acid. These were then collected and grouped according to their chromatographic profile and the eluent was removed by vacuum evaporation. The fractions obtained were weighed and labelled from XA_1 to XA_{10}. XA_1, XA_3 , XA_6 , XA_7 , were selected for purification based on their mass and TLC profile. Each of these fractions was applied to a second or third column and eluted with a gradient of dichlorometan/ethyl acetate in the ration of v/v (80/20). The pure products obtained are: $XA_{1.1}$; $XA_{3.4}$, $XA_{6.2}$; and $XA_{7.3}$.

NMR analysis of the isolated compounds: 1D and 2D NMR spectra were recorded using a BrukerAvance 400 MHz spectrometer. Chemical shifts are expressed in ppm. The solvent used was deuterated acetone (δH=2.17ppm; δC=207ppm).

RESULTS AND DISCUSSION

Compound 1 ($XA_{1.1}$): Compounds 1(23 mg) was isolated from X_{A1}(210mg) as a yellow oil. Its ^1H NMR (Figure 2) has revealed a simple aromatic system.

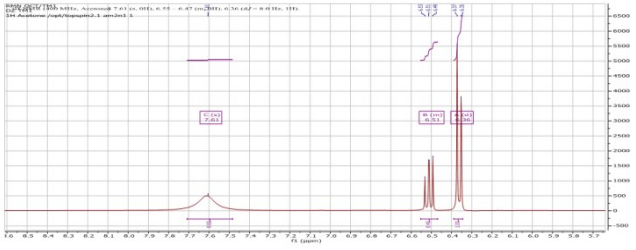
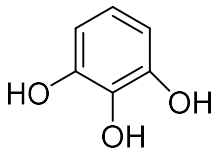


Figure 2.NMR^1**H of XA $_{1.1}$**

A doublet at 6.36ppm with coupling constants of 8Hz characteristic of a $^3J_{HH}$, integrating for two protons, a triplet at 6.51ppm integrating for 1H and a singlet at 7.61ppm integrating for 3H (OH) are observed in this spectrum.

Table 1. Comparison of ^1H chemical shifts in ppm of XA_1 with the literature

Nature	1H assigned to compound 1 δ (ppm)	Literature δ(ppm)	Difference Δδ(ppm)	Multiplicity
$^{4,6}H$	6,36	6,31	0,05	d
^{5}H	6,51	6,51	0,00	t
$^{1, 2,3H}$(OH)	7,61			s



Compound 1. Pyrogallol

These signals correspond to a tri-substituted benzene. These shifts are similar to those of pyrogallol (Table1) (Honda and Masuda, 2016).

Compound 2 ($XA_{4.3}$):Compound 2(12mg) was isolated in XA_2(920mg) as a dark orange oil. Analysis of the ^1H NMR indicates the characteristics of a di-substituted benzene AB_2 with two hydroxyl groups. Comparison of the chemical shift in ppm of the putative molecule confirms that it is catechol (Kametani et *al*., 2007) (Table 2).

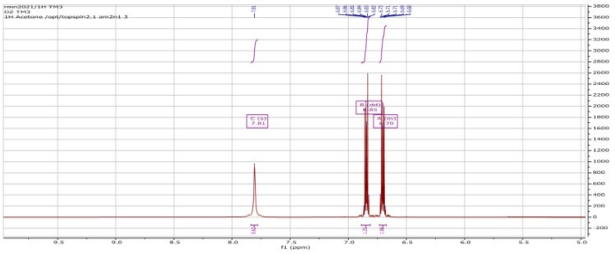
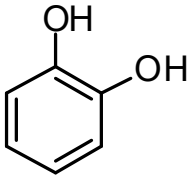


Figure 3. **RMN ^{1}H of $XA_{3.4}$**

Table 2. Comparison of ^1H chemical shifts in ppm of XA_1 with the literature

Nature	Protonassigned to compound 1 δ (ppm)	Literature δ (ppm)	Difference Δδ (ppm)	Multiplicity
$^{4,5}H$	6,70	6,52	0,18	dd
$^{3,6}H$	6,85	6,81	0,04	dd
$^{1,2}OH$	7,81	7,79	0,02	s



Compound 2. Catechol

Compound 3 ($XA_{6.2}$):Compound 3 is in the form of an oily beige compound soluble in acetone. It is visible in UV 254 nm on TLC plate.

Analysis of the ^1H NMR spectrum (Figure 4) shows:

- A peak at δ_H 7.92 ppm attributable to a hydroxyl group;
- An aromatic proton at δ_H7.47 ppm (dd, ^3J = 8.20Hz and 4J = 2Hz) coupling with two other aromatic protons in ortho and meta;
- An aromatic proton at δ_H 7.50 ppm (d, ^4J = 2Hz) coupling in meta;
- An aromatic proton at δ_H 6.89 ppm (d, ^3J = 8.20Hz) coupling in ortho;

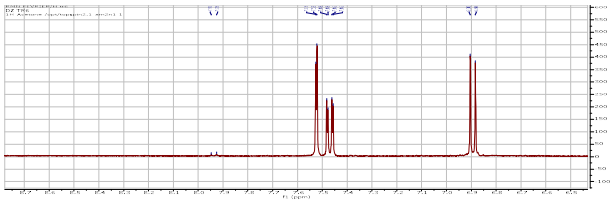


Figure 4. A: NMR[1]H of compound 3($XA_{6.2}$)

A total of three aromatic protons in the ^{1}H NMR spectrum suggest a trisubstituted benzene ring.

The ^{13}C NMR spectrum shows (Figure 5)

- 3 aromatic CH C-H resonating at 150.7, 145.5 and 123
- 3 quaternary carbons at 123.5, 117.4 and 115.6 ppm
- an acidic carbonyl at 167.7.

These CHs are similar to the 2CH, 5CH, 6CH of protocatechic acid (Gutzeit et al., 2007).Based on the proton integrals with their coupling constant and carbon number, this suggests a trisubstituted aromatic ring with one COOH carboxylic acid group and two OH hydroxyl groups as substituents.

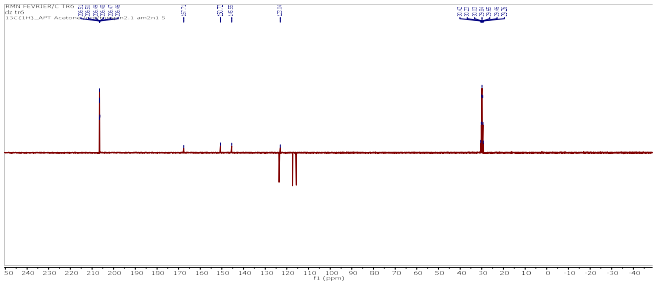
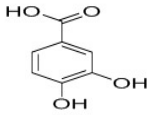


Figure 5. RMN ^{13}C of Compound 3 ($XA_{6.2}$)



Compound 3.Protocatechiuc acid

Compound 4 ($XA_{7.3}$)

Analysis of the ^{1}H NMR spectrum:The compound 4 isolated in the XA_7 fraction has the flavan-3-ol unit shown below (Figure 6). The proton spectrum consists of 3 characteristic subspectra.

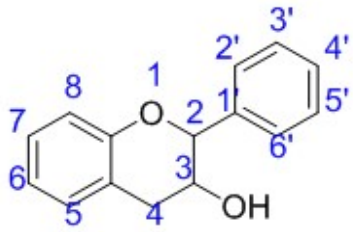
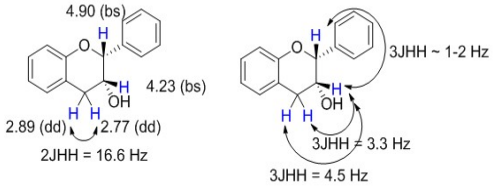


Figure 6. Flavan-3-ol motif and numbering of the different atoms

The aliphatic unit consists of 4 protons and a CHCHCH2 chain. The characteristic signals have chemical shifts of 4.90 ppm for proton 2, 4.23 ppm for proton 3 and 2.89 and 2.77 ppm for the protons of methylene group 4 (Figure 7). It can be noted that the flavan-3-ol unit has two stereogenic centres 2C-H and 3C-H. Therefore, the protons of methylene 4 are diastereotopic. They have different chemical shifts and have a geminal coupling constant ^{2}JHH equal to 16.6 Hz.



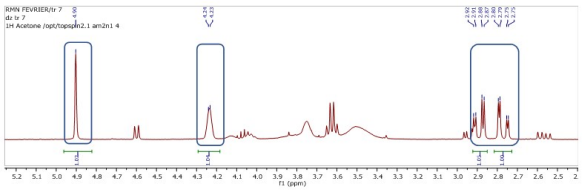


Figure 7.[1]H NMR of the aliphatic part of the isolated product

This coupling constant value is very sensitive to the chemical environment, but as can be seen in the figure below (Figure 3) giving coupling constant values for different environments, it is relatively large in absolute value for the six-membered rings (13.0 Hz) and consistent with that observed.

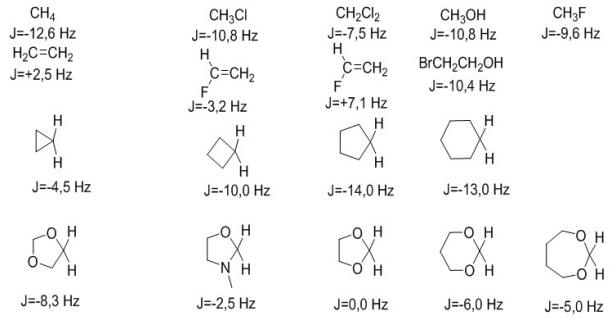


Figure 8. Geminal coupling constants of some characteristic systems

The vicinal coupling constants provide more information on the relative stereochemistry of the two stereogenic centres of the flavan-3-ol unit. Indeed, the $^{3}J_{HH}$ are strongly influenced by the dihedral angle. They generally obey the Karplus relationship. The Karplus equation shows that anti-periplanar protons have the largest coupling constants, while protons with dihedral angles between 60° and 120° have the lowest ^{3}J values. Thus, in the six-membered rings it is very easy to distinguish axial vicinal protons (coupling constant greater than 8 Hz). The other vicinal interactions generally have lower J values, between 0 and 5 Hz ($J_{\text{axial-equatorial}}$ and $J_{equatorial\text{-}equatorial}$).

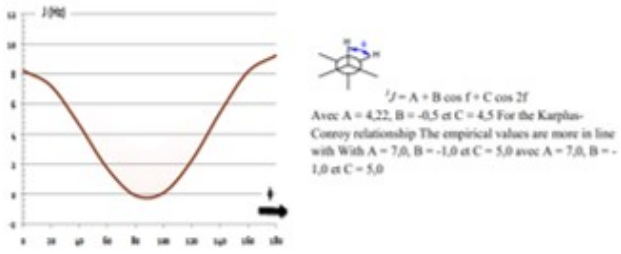


Figure 9.Karplus relationship and vicinal coupling constant ^{3}JHH

If we look at the two relative configurations of the flavan-3-ol systems, we can have the cis and trans systems. If we consider that the most voluminous group (Ar) is in the equatorial position, the conformation adopted for each of the systems leads to having the

proton in position 3 respectively in the equatorial position for the cis system and in the axial position for the trans system. Consequently, the proton 3 must have:

- 2 $J_{axial\text{-}equatorial}$ coupling constants and 1 Equatorial-equatorial coupling constant) for the cis system,
- 2 $J_{axial\text{-}axial}$ coupling constants and 1 Equatorial-axial coupling constant) for the cis system.

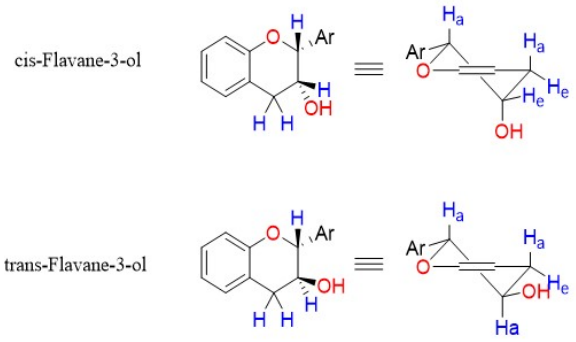


Figure 10. Conformations of the cis- and trans-flavan-3-ol systems.

In the isolated molecule, the coupling constants between proton 3 and the protons of the methylene group at position 4 are 4.5 and 3.3 Hz. This corresponds to a cis-flavan-3-ol unit.

- The rest of the proton spectrum is made up of two aromatic systems. The first (part A) gives two doublets at 6.05 and 5.95 ppm with a coupling constant J = 2.2 Hz respectively. This is therefore a tetrasubstituted aromatic system with the two protons placed in a Meta position relative to each other. Their very low chemical shift is compatible with the 6 and 8 protons of epicatechin.
- Similarly, the signals at 7.08, 6.86 and 6.81 ppm correspond to a trisubstituted aromatic system with two protons in the ortho position and the last one in the meta and para positions relative to the first two. Their chemical shift is compatible with the 2', 5' and 6' protons of epicatechin.

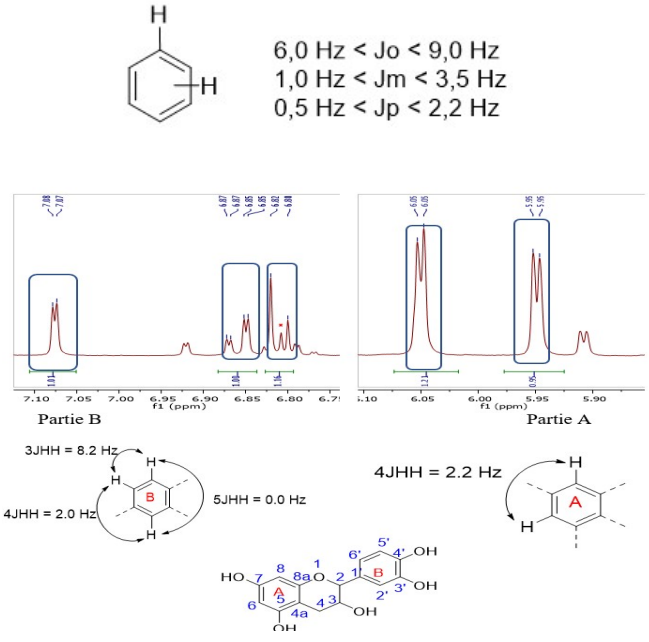


Figure 11. ^{1}H NMR of aromatics proton and epicatechin structure

Analysis of the ^{13}C NMR spectrum: The ^{13}C NMR spectrum using the APT (Attached Proton Test) technique. It combines some of the advantages of a DEPT, phase separation based on the number of hydrogen atoms attached to the corresponding carbon and the presence of quaternary carbons. It is shown in Figure 12.

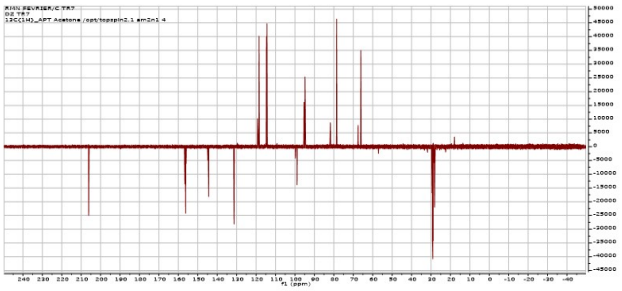


Figure12.^{13}C NMR spectrum of compound 4

If the assumed structure is indeed that corresponding to epicatechin, the carbon spectrum should show some characteristic NMR signals:

- The presence of 3 aliphatic carbons: 4CH2 has been unambiguously assigned with δC=29.1 ppm is the least deblocked. The 2CH and 3CH are 78.5 ppm and 66.1 ppm respectively. The chemical shifts of these carbons are similar to those observed by El-Razek et *al* (2015) in his publication on flavan-3-ol systems. In particular for epicatechin with chemical shifts of δC4=29.0; δc3=67.0 and δC2=79.5 ppm in acetone-d6 as solvent.

- The aromatic systems are more complex and have quaternary carbons and CHs. We therefore had to assign CHs for each of the aromatic systems. For ring A there are two CHs, 6CH and 8CH and for ring B there are three aromatic CHs (2'CH, 5'CH, 6'CH). We were able to assign each of these signals. Carbons 6 and 8 are strongly shielded for sp2 carbons and resonate at 95.3 and 94.8 ppm. The 2'CH, 5'CH, 6'CH carbons of ring B resonate at 114.4, 114.7 and 118.5 ppm. Their low chemical shift is also characteristic of an aromatic system with donor groups.
- Aromatic systems also consist of seven quaternary carbons. They can be divided into two groups: those linked to a heteroatom (oxygen) and those linked to a carbon atom. The latter are less unbundled than the former. Their chemical shift is 98.9 and 131.3 ppm for 4aC and 1'C respectively. As regards the sp^2 carbons linked to oxygen, the carbons concerned are carbons 5, 7, 8a, 3' and 4' and their chemical shifts are 156.7, 156.6, 144.5 and 144.4 ppm.

It should be noted that for the latter the assignment was made by analogy with literature data. As can be seen in Table 6, the differences in chemical shift between the literature data and our isolated compound (compound 4) do not exceed 0.3 ppm (Vdovin et *al*., 1997).Compounds 1, 2, 3 and 4 isolated from the acetate extract of *X. americana* trunk bark, and identified as: pyrogallol, catechol, protocatechic acid and epicatechin respectively, by comparison of ^{1}H and ^{13}C NMR with those of authentic spectra from the literature. These compounds were isolated and identified for the first time from the trunk bark of *X. americana*. The antioxidant properties of pyrogallol (Kulkarni and Suzuki, 2008), protocatechic acid (Wang et al., 2011) and epicatechin (Ana Lúcia andGalotta, 2008) have been reported. Catechol induces the activities of antioxidant enzymes (catalase, superoxide dismutase, peroxidase, glutathione S-transferase, glutathione peroxidase and glutathione reductase) (jiang et al., 2018). Epicatechin also has anti-hypertensive properties, causing an increase in NO in the vascular system when pressure is increased (Galleano et *al*., 2010), (Gomez-Guzman et *al*., 2012). Buijsse et *al* (Buijsse et *al*., 2010) have shown that epicatechin reduces blood pressure by an average of 4.1 and 2.0 mmHg systolic and diastolic blood pressure, respectively (Elinjer et al., 2012); improves myocardial stiffening (Jackson D. et al., 2018).

Table 3: Comparison of ^{1}H chemical shifts in ppm of compound 3 with the literature

Nature	^{1}H assigned to compound 3 δ (ppm)	Literature δ (ppm)	Difference Δδ (ppm)	Multiplicity
^{2}H	7,50(J=2Hz)	7,44(J=1,5Hz)	0,06	d
^{5}H	6,89(8,2Hz)	6,78 (8Hz)	0,09	d
^{6}H	7,47(J=8,3-2Hz)	7,41(1,5-8,4 Hz)	0,03	dd

Table 4: Comparison of ^{13}C chemical shifts in ppm of compound 3 with the literature

Nature	^{13}C assigned to compound 3 δ (ppm)	^{13}C assigned to protocatechuic acid δ (ppm)	DifferenceΔδ (ppm)
^{1}C-H	123,5	123,7	0,2
^{2}C-H	117,4	117,7	0,3
^{3}C	145,5	146	0,5
^{4}C	150,7	151,3	0,6
^{5}C	115,6	115,7	0,1
^{6}C-H	123,5	123,9	0,4
C=O	167,7	170,5	2,8

Table 5: Comparison of ^{1}H chemical shifts in ppm of compound 4 with the literature.

Nature	^{1}H assigned to compound 4 δ (ppm)	^{1}H assigned to epicatechin δ (ppm)	Difference Δδ (ppm)	Multiplicity
^{2}H	4.90	4,88	0,02	(s, 1H, CH),
^{3}H	4.23	4,21	0,02	(bs, 1H),
$^{4}H_{axi}$	2.89	2,87	0,02	(dd, *J* = 16.6 1H, CH_2)
$^{4}H_{eq}$	2.77	2,74	0,02	(dd, *J* = 16.6, 1H, CH_2)
^{6}H	6.05	6,02	0,03	(d, *J* = 2.2 Hz, 1H, CH),
^{8}H	5.95	5,92	0,03	(d, *J* = 2.3 Hz, 1H, CH)
$^{2'}$CH	7.08	7,05	0,03	(d, *J* = 2.0 Hz, 1H, CH),
$^{5'}$CH	6.81	6,79	0,02	(d, *J* = 8.1 Hz, 1H, CH),
$^{6'}$CH	6.86	6,84	0,20	(dd, *J* = 8.2, 1H, CH)

Table 6: Comparison of ^{13}C chemical shifts in ppm of compound 4 with the literature

Nature	^{13}C chemical shift of compound 4 (ppm)	^{13}C assigned to epicatechin	Δδ (ppm)
^{2}CH	79,3	79,5	0,2
^{3}CH	66,9	67,0	0,1
$^{4}CH_2$	28,9	29,0	0,1
^{4a}C	99,7	100,0	0,3
^{5}C	157,5	157,6	0,1
^{6}CH	96,1	96,2	0,1
^{7}C	157,4	157,6	0,2
^{8}CH	95,6	95,7	0,1
^{8a}C	157,0	157,2	0,2
$^{1'}$C	132,1	132,3	0,2
$^{2'}$CH	115,2	115,3	0,1
$^{3'}$C	145,3	145,4	0,1
$^{4'}$C	145,2	145,3	0,1
$^{5'}$CH	115,4	115,5	0,1
$^{6'}$CH	119,2	119,4	0,2

CONCLUSION

The purification of phenolic compounds from the ethyl acetate extract of X. americana trunk bark allowed to obtain ten fractions coded as XA1 to XA10. From subfractions of XA1, XA3, XA6 and XA7 we have isolated respectively and determined the structure of, pyrogallol, catechol, protocatechiuc acid and epicatechin. The first three compounds were identified for the first time in the bark of this plant. The presence of these compounds provides a strong scientific basis for the view that X. americana trunk bark is rich in phenolic compounds with antioxidant properties that have been proven in the literature.

Acknowledgements

The author thanks the Service de Cooperation and cultural Action (SCAC) of the French Embassy in Niger for the financial support and the Laboratory of Molecular Architecture and Nanostructured Materials (AM2N) of the Charles Gerhardt Institute of Montpellier (ICGM) for having accepted me in their team.

REFERENCES

ABD EL-Razek M.H. (2007), NMR Assignments of Four CatechinEpimers, Asian Journal of Chemistry, Vol. 19, No. 6, 4867-4872.

Andrea G., Erik I. (2015) 5 year mortality predictors in 498 103 UK Biobank participants: aprospectivepopulation-based study. Lancet; 386: 533-40, http://dx.doi.org/10.1016/ S014 6736(15)60175-1

Aissa M.J., Karim S., Morou B., Rokia S. ;, et Mahamane S. (2017), « Enquête Ethnobotanique Auprès Des Tradipraticiens De Santé Des Régions De Niamey Et Tillabéry Au Niger:Données 2012-2017 », Eur. Sci.J. ESJ, vol. 13, n° 33, p. 276, Doi: 10.19044/esj.2017.v13n33p276

Ana Lúcia Q. A. Galotta (2008). Antioxidant and cytotoxic activities of 'AÇAÍ' (Euterpeprecatoria Mart.), Quim. Nova, Vol. 31, No. 6, 1427-1430

Bruno B. (2020). Stress oxydant et protections antioxydantes. Revue francophone des laboratoires, N °522

Buijsse B., Weikert C., Drogan D, Bergmann M., Boeing H. (2010): Chocolate consumption in relation to bloodpressure and risk of cardiovascular disease in German adults. *Eur Heart J*, 31:1616-1623

Ellinger S, Reusch A, Stehle P, Helfrich HP (2012), Epicatechin ingested via cocoa products reduces blood
pressure in humans: a non linear regression model with a Bayesian approach. *Am J ClinNutr*, 95:1365-1377.

Galleano M., Pechanova O., et C. G. Fraga (2010), « Hypertension, Nitric Oxide, Oxidants, and Dietary Plant
Polyphenols » Curr.Pharm. Biotechnol., vol. 11, n° 8, p. 837-848, doi10.2174/138920110793262114

Gómez-Guzmán M., Jiménez R., Sánchez M., Zarzuelo M J, Galindo P., Quintela AM., López-Sepúlveda R., l

Romero M, Tamargo Juan, Vargas Félix, Pérez-Vizcaíno F, Duarte J. (2012); Epicatechin lowers bloodpressure, restores endothelial function, and decreases oxidative stress and endothelin-1 and NADPHoxidase activity in DOCA-salt hypertension, *Free Radical Biology & Medicine* 52 , 70–79

Helmut M. H., Neale Jackson, Brian May, Anthony L. Zhang, Charlie C. Xue (2016). Polyphenol protection and treatment of hypertension.Phytomedicine 23, 220–231

GutzeitD ., V Wray., Winterhalter P., Jerz G,. (2007), Preparative Isolation and Purification of Flavonoids and
Protocatechuic Acid from Sea Buckthorn Juice Concentrate (Hippophae¨ rhamnoides L. ssp. rhamnoides)by High-Speed Counter-Current Chromatography, Chromatographia 65, (No. 1/2) DOI: 10.1365/s10337-006-0105-60009-5893/07/01.

Honda S. and MasudaT. (2016), Identification of Pyrogallol in the Ethyl Acetate-Soluble Part of Coffee as the Main Contributor to Its Xanthine Oxidase Inhibitory Activity, J. Agric. Food Chem. 2016, 64, 7743-7749, DOI: 10.1021/acs.jafc.6b03339.

Jackson, D.; Connolly K.; Batacan, R.; Ryan, K.; Vella, R.; Fenning, Andrew. 2018."(−)-Epicatechin Reduces
Blood Pressure and Improves Left Ventricular Function and Compliance in Deoxycorticosterone Acetate
Salt Hypertensive Rats" Molecules 23, no. 7: 1511. https doi.org/10.3390/molecules23071511

Jiménez R., López-SepúlvedaRocío, Kadmiri M., Romero M.,
R. Vera, Sánchez, M. Vargas F., O'Valle F.,
Zarzuelo A., M Dueñas., Santos-Buelga C., Duarte J. (2007). Polyphenols restore endothelial function in
DOCA-salt hypertension: Role of endothelin-1 and NADPH oxidase. Free Radical Biology & Medicine 43, 462–473

Kametani S., Yuasa A k, kizokaki H, Kennedy D.O., Honzawa M, Matsui-Yasa I. Chemical constituents of cape
and their synergic-growth inhibition effect on Ehrlich Ascites tumor cells. Biosci.biotechnol.Biochem, 71(5), 1220-1229

KulkarniA ., Hideo S.S. (2008), Antioxidant compounds from Eucalyptus grandis biomass by subcritical liquid
water extraction, The Japan Wood Research Society, 54:153-157 DOI 10.1007/s10086-007-0916-6

Le N. H. T., Mattered K. E.,Diallo D., Paulsen B. S., Nergard C. S., et Wangensteen H. (2012), « Bioactivepolyphenols in Ximeniaamericana and the traditional use among Malian healers », J. Ethnopharmacol., vol. 139, n° 3, p. 858-862, févr. 2012, doi: 10.1016/j.jep.2011.12.031.

Li X., Wang X., Chen D., et Chen S. (2011), « Antioxidant Activity and Mechanism of Protocatechuic Acid in vitro », Funct. FoodsHealth Dis., vol. 1, n° 7, p. 232, doi: 10.31989/ffhd.v1i7.127.

Ministère de la sante publique (2008). Mesure des facteurs de risque des maladies non transmissibles Au Niger(Approche Step"wise" de l'OMS

Moreno-Luna R., Muñoz-Hernandez R., Miranda M. L., Costa A. F., Jimenez-Jimenez L., Vallejo-Vaz A. J., Muriana F. J.G., Villar J., StiefelP. (2012). Olive Oil Polyphenols Decrease Blood Pressure and Improve Endothelial Function in Young Women with Mild Hypertension.american journal of hypertension volume25,1299-1304.

N'guessan H. A .,Déliko Camille Evelyne Dago, Mamyrbékova-Békro J.A, Béhro Y (2011). CCM d'extraits
sélectifs de 10 plantes utilisées dans le traitement traditionnel de l'hypertension artérielle en Côte d'Ivoire.European Journal of Scientific Research, EuroJournals, 66 (4), pp.575-585, hal-01447284.

Vdovin A. D., Kuliev Z. A., et Abdullaev N. D. (1997), « ^{1}H AND ^{13}C spectroscopy in the study of flavan-3- ols, proanthocyanidins, and their derivatives » .Chemistry of natural compounds, 33,11-24

Shaofeng J., Chenjiaozi W., Canwei S., Yongkun H., Mei Y. &Erxun Z. (2018): Effects of catechol on growth, antioxidant enzyme activities and melanin biosynthesis gene expression of Rhizoctoniasolani AG-1 IA, Canadian Journal of Plant Pathology, DOI: 10.1080/07060661.2018.1437775

Yousepan M., Shakour N., HosseinHosseinzadeh, A.Wallace Hayes, FarzinHadizadeh, GholamrezaKarimi (2018), The natural phenolic compounds as modulators of NADPH oxidases inhypertension.Phytomedecine, 52583, 1-38.

****