Published in final edited form as:

Nat Prod Res. 2019 January ; 33(2): 287–291. doi:10.1080/14786419.2018.1440225.

Chemical and biological studies on *Bridelia ferruginea* grown in Nigeria

Michael Afolayan^{a,b,c}, Radhakrishnan Srivedavyasari^a, Olayinka T. Asekun^b, Oluwale B. Familoni^b, and Samir A. Ross^{a,d}

^aNational Center for Natural Product Research, University of Mississippi, University, MS, USA

^bDepartment of Chemistry, University of Lagos, Lagos, Nigeria

^cChemistry Advanced Research Center, Sheda Science and Technology Complex, Garki-Abuja, Nigeria

^dDepartment of BioMolecular Sciences, School of Pharmacy, University of Mississippi, University, MS, USA

Abstract

Phytochemical investigation of the methanolic extract of dried leaves of *Bridelia ferruginea* led to the isolation and identification of fourteen compounds (**1–14**): compound **1** [mixture of palmitic, stearic and oleic acids], stearyl monoester of 2-*O*- β -D-glucosylglycerol (**2**), 6 β -hydroxy-(20*R*)-24-ethylcholest-4-en-3-one (**3a**), 6 β -hydroxy-(20*R*)-24-ethylcholest-4,22-dien-3-one (**3b**), lutein (**4**), vomifoliol (**5**), corilagin (**6**), kaempferide-3-*O*- β -D-glucoside (**7**), myricetin (**8**), isomericitrin (**9**), isoquercetin (**10**), myricitrin (**11**), quercitrin (**12**), rutin (**13**), and β -sitosterol glucoside (**14**). The total extract exhibited moderate activity towards CB2 receptor and 90% inhibition against leishmanial pathogen *Trypanosoma brucei*. Compound **4** exhibited 73% displacement in CB2 receptor with IC₅₀ 56.47 μ M, and 93% inhibition towards *T. brucei* with IC₅₀ 4.16 μ M. Compound **11** showed 99% inhibition towards *Escherichia coli* with IC₅₀ 1.123 μ M.

Graphical abstract

Keywords

Bridelia ferruginea; flavonoids; cannabinoid receptor; antileishmanial; antibacterial

CONTACT Samir A. Ross, sross@olemiss.edu.

Supplemental data for this article can be accessed at <https://doi.org/10.1080/14786419.2018.1440225>.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Radhakrishnan Srivedavyasari ^{iD} <http://orcid.org/0000-0001-9495-7169>

1. Introduction

Bridelia ferruginea (Euphorbiaceae) commonly found in Savannah regions, is usually a gnarled shrub which sometimes reaches the size of a tree. This plant in Southern Nigeria is considered as sacred and is featured in certain rituals and ceremonies. It is used as ethnomedicine for treatment of various ailments in many parts of Africa. The bark, roots, fruits and leaves decoctions are used mainly as purgative and a vermifuge (Cimanga et al. 1999; Okwu and Ukanwa 2010; Mbah et al. 2012). Previous biological studies showed that crude extracts of this plant has capability to lower the fasting blood sugar levels of rats and humans, also used to cure piles, diarrhea, female sterility, rheumatic pains (Mostafa et al. 2006; Pettit et al. 2016), intestinal and bladder disorders, skin diseases, dysentery, and elephantiasis of the scrotum (Bruyne et al. 1997). Other reported activities of the bark extract include antineuroinflammatory (Olajide et al. 2012), typanocidal (Ekanem et al. 2008), antioxidant (Oloyede and Babalola 2012), antimicrobial (Adeoye et al. 1988), antimolluscidal, anti-inflammatory (Olajide et al. 1999), analgesic and antipyretic properties (Akuodor et al. 2011). *B. ferruginea* plant is reported to contain tannins and flavonoids (Oliver-Bever 1986; Addae-Mensah and Munenge 1989; Bruyne et al. 1997; Cimanga et al. 1999, 2001; Rashid et al. 2000; Okwu and Ukanwa 2010). Based on traditional medicinal uses, previous reported activities and our crude extract showed moderate activity towards CB2 receptor and potent against leishmanial pathogen encouraged to study the cannabinoid, opioid receptors and antileishmanial activities for the compounds isolated from *B. ferruginea*.

2. Results and discussion

Phytochemical investigation of the methanolic extract of dried leaves of *B. ferruginea* led to the isolation of fourteen compounds (**1–14**, Figure 1). The isolated compounds were identified by their NMR, MS and GC-MS spectral data analyses. Compound **1** (oily mass), further analysis by GC MS was identified to be a mixture of three fatty acids [palmitic (53.5%), stearic (16.2%) and oleic (14.3%)]. A fatty acid monoester of 2-*O*- β -D-glucosylglycerol (**2**) (Colombo et al. 1996), the fatty acid was identified by using GC-MS to be stearic acid. Compound **3** was found to be a mixture of 6 β -hydroxy-(20*R*)-24-ethylcholest-4-en-3-one, (**3a**), as major and 6 β -hydroxy-(20*R*)-24-ethylcholest-4,22-dien-3-one (**3b**) as minor (Kontiza et al. 2006), lutein (**4**) (Moss 1976), vomifoliol (**5**) (Hammami et al. 2004), corilagin (**6**) (Moreira et al. 2013), kaempferide-3-*O*- β -D-glucoside (**7**) (Lee et al. 2008), myricetin (**8**) (Zhang et al. 2011), isomyricetin (**9**), isoquercetin (**10**) (Ren et al. 2012), myricitrin (**11**) (Aderogba et al. 2013), quercitrin (**12**), rutin (**13**) (Zhang et al. 2014), β -sitosterol glucoside (**14**).

The total extract exhibited moderate activity towards CB2 receptor (48% displacement) and 90% inhibition towards *Trypanosoma brucei* with IC₅₀ 8.48 μ M. Lutein (**4**) exhibited 73% displacement in CB2 receptor with IC₅₀ 56.47 μ M (Figure 2) and moderate activity in Delta and Mu opioid receptors (65% and 49% displacement, respectively). Also **4** showed 93% activity against *T. brucei* (IC₅₀ 4.16 μ M) and moderate activity towards *Leishmania donovani* (48%, IC₅₀ 9.3 μ M). Myricitrin (**11**) showed 99% inhibition towards *Escherichia coli* Pinh with IC₅₀ 1.123 μ M.

3. Conclusion

The methanolic extract of dried leaves of *B. ferruginea* showed 90% activity towards *T. brucei* and moderate activity (48% displacement) towards CB2 receptor. Bioassay guided fractionation and purification yielded fourteen compounds (1–14). Compounds 2–7, 9, and 12 were reported for the first time from this plant. Lutein (4) exhibited strong activity towards CB2 receptor and leishmanial pathogen *T. brucei*. Myricitrin (11) exhibited potent activity towards *E. coli* Pinh.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The project was supported by Sheda Science and Technology Complex, Nigeria and National Center for Natural Product Research, USA. We acknowledge Award number P20GM104932 from the National Institute of General Medical Sciences for bioassay results.

Funding

This work was supported by the National Institute of General Medical Sciences [grant number P20GM104932].

References

- Addae-Mensah I, Munenge RW. 1989; Quercetin 3-neohesperidoside (rutin) and other flavonoids as the active hypoglycemic agents of *Bridelia ferruginea*. *Fitoterapia*. 60:359–362.
- Adeoye, AO, Abaeli, AM, Owowumi, CJ, Olukoya, DK. Book of abstract of the symposium on drug production from natural products. Drug Research and Production Unit, Obafemi Awolowo University; Ile-Ife: 1988. Antimicrobial activity of *Bridelia ferruginea*; 24
- Aderogba MA, Ndhlala AR, Rengasamy KRR, Van Staden JV. 2013; Antimicrobial and selected in vitro enzyme inhibitory effects of leaf extracts, flavonols and indole alkaloids isolated from *Croton menyharthii*. *Molecules*. 18:12633–12644. [PubMed: 24126380]
- Akuodor GC, Mbah CC, Anyalewechi NA, Idris-Usman M, Iwuanyanwu TC, Osunkwo UA. 2011; Pharmacological profile of aqueous extract of *Bridelia ferruginea* stem bark in the relief of pain and fever. *J Med Plants Res*. 5:5366–5369.
- Bruyne T, Cimanga K, Pieters L, Claeys M, Dommissie R, Vlietinck A. 1997; Gallocatechin – (4'→0→7)-epigallocatechin, a new biflavonoid isolated from *Bridelia Ferruginea*. *Nat Prod Let*. 11:47–52.
- Cimanga K, De Bruyne T, Apers S, Dieters L, Totté J, Kambu K, Tona L, Bakana P, van Ufford LQ, Beukelman C, et al. 1999; Complement-inhibiting constituents of *Bridelia ferruginea* stem bark. *Plant Med*. 65:213–217.
- Cimanga K, Ying L, De Bruyne T, Apers S, Cos P, Hermans N, Bakana P, Tona L, Kambu K, Kalenda DT, et al. 2001; Radical scavenging and xanthine oxidase inhibitory activity of phenolic compounds from *Bridelia ferruginea* stem bark. *J Pharm Pharmacol*. 53:757–761. [PubMed: 11370716]
- Colombo D, Ronchetti F, Scala A, Taino IM. 1996; A facile lipase catalyzed access to fatty acid monoesters of 2-O-β-D-glucosylglycerol. *Tetrahedron: Asymmetry*. 7:771–777.
- Ekanem JT, Kolawole OM, Abbah OC. 2008; Trypanocidal potential of methanolic extracts of *Bridelia ferruginea* benth bark in *Rattus novergicus*. *Afr J Biochem Res*. 2:045–050.
- Hammami S, Jannet H, Bergaoui A, Ciavatta L, Cimino G, Mighri Z. 2004; Isolation and Structure Elucidation of a Flavanone, a Flavanone Glycoside and Vomifoliol from *Echiochilon Fruticosum* Growing in Tunisia. *Molecules*. 9:602–608. [PubMed: 18007460]

- Kontiza I, Abatis D, Malakate K, Vagias C, Roussis V. 2006; 3-Keto steroids from the marine organisms *Dendrophyllia cornigera* and *Cymodocea nodosa*. *Steroids*. 71:177–181. [PubMed: 16280145]
- Lee E, Moon B-H, Park Y, Hong S, Lee S, Lee Y, Lim Y. 2008; Effects of hydroxy and methoxy substituents on NMR data in flavonols. *Bull Korean Chem Soc*. 29:507–510.
- Mbah CC, Akuodor GC, Anyalewechi NA, Iwuanyanwu TC, Osunkwo UA. 2012; In vivo antiplasmodial activities of aqueous extract of *Bridelia ferruginea* stem bark against *Plasmodium berghei berghei* in mice. *Pharm Biol*. 50:188–194. [PubMed: 22235887]
- Moreira J, Klein-Júnior LC, Filho V, de Campos Buzzi F. 2013; Anti-hyperalgesic activity of corilagin, a tannin isolated from *Phyllanthus niruri* L. (Euphorbiaceae). *J Ethnopharmacol*. 146:318–323. [PubMed: 23333746]
- Moss GP. 1976; Carbon-13 NMR Spectra of Carotenoids. *Pure & App Chem*. 47:97–102.
- Mostafa M, Nahar N, Mosihuzzaman M, Sokeng SD, Fatima N, Atta-ur-Rahman, Choudhary MI. 2006; Phosphodiesterase-I inhibitor quinovic acid glycosides from *Bridelia ndellensis*. *Nat Prod Res*. 20:686–692. [PubMed: 16901813]
- Okwu DE, Ukanwa N. 2010; Isolation and characterization of flavonoids chalcones and anthocynidines from *Bridelia ferruginea* benth. *Der Chemica Sinica*. 1:21–28.
- Olajide OA, Makinde JM, Awe SO. 1999; Effect of aqueous extract of *Bridelia ferruginea* stem bark carrageenan-induced oedema and granuloma tissue formation in rats and mice. *J Ethnopharmacol*. 66:113–117. [PubMed: 10432217]
- Olajide OA, Aderogba MA, Okorji UP, Fiebich BL. 2012; *Bridelia ferruginea* produces antineuroinflammatory activity through inhibition of nuclear factor-kappa B and p38 MAPK signaling. *Evid Based Complement Alternat Med*. :8.
- Oliver-Bever B. 1986; Medicinal plants in tropical West Africa. Cambridge. :258–260.
- Oloyede OI, Babalola SO. 2012; *In-vitro* antioxidant activity of ethanolic extract of *Bridelia ferruginea*. *J Acad Res Int*. 2:246–251.
- Pettit GR, Searcy JD, Tan R, Cragg GM, Melody N, Knight JC, Chapuis JC. 2016; Antineoplastic agents. 585. Isolation of *Bridelia ferruginea* anticancer podophyllotoxins and synthesis of 4-azapodophyllotoxin structural modifications. *J Nat Prod*. 79:507–518. [PubMed: 26938998]
- Rashid MA, Gustafson KR, Cardellina JH, Boyd MR II. 2000; A new podophyllotoxin derivative from *Bridelia ferruginea*. *Nat Prod Let*. 14:285–292.
- Ren G, Hou J, Fang Q, Sun H, Liu X, Zhang L, Wang PG. 2012; Synthesis of flavonol 3-O-glycoside by UGT78D1. *Glycoconj J*. 29:425–432. [PubMed: 22767031]
- Zhang S, Lu W, Liu X, Diao Y, Bai F, Wang L, Shan L, Huang J, Li H, Zhang W. 2011; Fast and effective identification of the bioactive compounds and their targets from medicinal plants via computational chemical biology approach. *Med Chem Commun*. 2:471–477.
- Zhang Y, Wang D, Yang L, Zhou D, Zhang J. 2014; Purification and characterization of flavonoids from the leaves of *Zanthoxylum bungeanum* and correlation between their structure and antioxidant activity. *PLoS ONE*. 9:e105725. [PubMed: 25157400]

Figure 1.
Compounds isolated from *B. ferruginea*.

Figure 2.
Binding summary of Lutein (4) towards CB2 receptor.