Funtulaticamide, a phytosphingosine-type ceramide from *Funtumia elastica* Preuss Stapf. (Apocynaceae) trunk bark with potential antileishmanial activity

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**ABSTRACT**

Phytochemical investigations of the trunk bark extract of *Funtumia elastica* (Preuss) Stapf, afforded a new ceramide namely, funtulaticamide (1) along with six known compounds: funtulatine (2), methyl ursolate (3), epicatechin (4), myricetin (5), sucrose (6) and 5-hydroxypyridine-3-carboxamide (7). Their structures were determined on the basis of various spectroscopic and chemical methods, as well as comparison with literature. Compounds were mostly isolated for the first time from this plant, and no evidence could be found on a previous report of a phytosphingosine-type ceramide in the genus *Funtumia*. Similarly, compound 7 is isolated from the Apocynaceae family for the first time. Hence, the chemophenetic significance of isolates was briefly introduced. In addition, compound 2 exhibited a moderate activity against *Leishmania donovani* 1S (MHOM/SD/62/1S) with an IC50 value of 15.9 μM.

# Subject and source

*Funtumia elastica* (Preuss) Stapf. (Apocynaceae) (also known as the bush rubber tree) is a medium-sized African rubber tree with glossy leaves and long woody seed pods (Blench, 2006), mostly found in central and western parts of Africa (Truong-Ho et al., 1963). Its stem bark is often used in pharmacopeia to treat whooping cough (Burkill, 1995), inflammatory diseases such as asthma, blennorrhea, and painful menstruation (Olaniyi, 1989), cutaneous fungal infections, hemorrhoids, syphilis, gonorrhea (Odugbemi, 2006; Burkill, 1995), wounds (Adekunle and Ikumapayi, 2006), snake bites and malaria (Betti al., 2004). The trunk bark of *F. elastica* (Preuss) Stapf, was collected in October 2019, in Mbankomo Sub-division (Ntouessong II Mountain, Centre Region (3° 25' 00" N, 11° 15' 00" E: Altitude 774 m). The plant material was identified by Mr. Tsambang Nole, Senior Scientific Officer, at the Institute of Medical Research and Medicinal Plants Studies, Yaounde, Cameroon. A voucher specimen (N° 59,012 HNC) was deposited at the National Herbarium in Yaounde, Cameroon.

# Previous work

Previous phytochemical investigations of *F. elastica* (leaves, stem bark, seeds) resulted in the isolation of steroidal alkaloids (Kom et al., 2021; Zirihi et al., 2005; Wagner et al., 1987; Tolela and Foche, 1979; Truong-Ho et al., 1963; Janot et al., 1963), triterpenoids (Kom et al., 2021; Mukam et al., 1973), a lactonic acid and sterols (Mukam et al., 1973) and a pyridine derivative compound (Kom et al., 2021). Recently, Frempong et al. (2021a) deduced that the total flavonoids content of the plant species was 78.0 ± 5.1 mg (QE/g of dried extract) in accordance with some results from Kom et al. (2021) who reported flavonol derivatives from the leaves of F. elastica. In continuation of our search for new biologically active compounds from this plant, we have investigated the trunk bark of the same plant collection, due to the fact that there is poor report about the chemical composition of this part of the plant species.

# Present study

## General experimental procedures

Optical rotations were measured on JASCO P-2100 polarimeter. UV and visible spectra were recorded in MeOH at 25 °C using a Kontron Uvikon spectrophotometer. The IR spectra were measured on a PerkinElmer 1750 FTIR spectrometer. 1D and 2D NMR spectra (1H and 13C, HSQC, HMBC, 1H-1H COSY and NOESY) were recorded in CDCl3 and/or MeOH-*d*4 on a Bruker 500 MHz NMR Avance II spectrometer equipped with a cryoprobe, with TMS as an internal reference. Melting points of the isolated compounds were determined using an Electro thermal IA9000 Series digital melting point apparatus (Bibby scientific, Great Britain). Chemical shifts (δ) were expressed in ppm with reference to TMS and coupling constants (*J*) were given in Hz. GC-MSD analyses were carried on a GCMS-QP2010SE (Shimadzu); HRESIMS spectra were determined on microTOF-focus and microTOF-Q III mass spectrometers (Bruker) and on Shimadzu LCMS-IT-TOF spectrometer (Kyoto, Japan). EI-MS was measured on Waters AutoSpec Premier P776 spectrometer. Analytical TLC were performed on precoated silica gel 60 F254 (Merck. 1.05735, Hohenbrunn, Germany) plates. After development ( *n*-hexane/EtOAc and/or CH2Cl2/MeOH, at different polarities), the dried plates were examined under short-wave (254 nm) or long-wave (366 nm) UV light. Liebermann-Burchard’s test and Dragendorff spray reagent were used for the staining of compounds on TLC silica gel plates. 0.036-0.071 mm (215-400 mesh) was used for CC with step gradients of *n*-hexane/EtOAc and CH2Cl2/MeOH as eluents respectively.

## Extraction and isolation

The trunk bark powder of *F. elastica* (1.5 kg) was soaked with CH2Cl2/MeOH (1:1) in a percolator at room temperature for 72 h. The extract was concentrated under vacuum and the residue (75 g, 5.0%) was obtained. A part of crude extract (70 g), was subjected to a gravity CC over silica gel by elution with CH2Cl2/MeOH in increasing order of polarity, to afford 5 fractions (A-E) according to TLC profile: fraction A [CH2Cl2 (100%)], fraction B [CH2Cl2/MeOH (5%-10%)], fraction C [CH2Cl2/MeOH (10%-20%)], fraction D [CH2Cl2/MeOH (20%-35%)] and fraction E [CH2Cl2/MeOH (35%-50%)]. The B2 subfraction (1.2 g), originating from fraction B (5.6 g), yielded compound 1 (19 mg) by elution with *n*-Hex/EtOAc (7:2) after repeated CC. Fraction C (8.5 g), was subjected to a silica gel CC using gradients of increasing amounts of MeOH (10-100%) in CH2Cl2, affording 4 subfractions (C1-C4). Subfraction C1 (258 mg) was subjected to a silica gel flash chromatography using *n*-hexane/EtOAc (9:1 to 3:1) to afford compounds 2 (22 mg) and 3 (5 mg). Subfraction E3 (600 mg), originating from fraction E (12 g), was subjected to a silica gel CC using gradients of increasing amounts of MeOH (10-100%) in CH2Cl2, yielding compounds 4 (8 mg) and 5 (9 mg). Purification of the remaining solid E4 (3.8 g, from fraction E under the same chromatographic conditions as already described, allowed the spectroscopic identification of compounds 6 (6.9 mg) and 7 (8.4 mg).

## Identification of compounds

Compound 1 was obtained as a white amorphous powder. The molecular formula C38H73NO4 was determined by the HR-ESI-MS *pseudo*-molecular ion peak at *m/z* 608.5689 (calcd for C38H74NO4, 608.5694 [M + H]+), suggesting three double bond equivalent (DBE). Its IR spectrum displayed characteristic absorption bands at 3420 cm-1 (hydroxy group), 2945 cm-1 (aliphatic C-H), 1652 cm-1 (olefinic group), 1637 cm-1 (amide carbonyl group), 1556 cm-1 (N-H bending) and 1027 cm-1 (hydroxy methine groups) (Ibrahim et al., 2008; Khedr et al., 2018). The 1H and 13C NMR spectra of 1 showed an amide proton at δH 7.32 (d, *J* = 9.0 Hz), three hydroxy groups at δH 5.56 (brs, 1-OH) and 5.75 (brs, 3, 4-OH), and two disubstituted olefinic bonds at δH/δC 5.36/129.5 and 5.36/131.1, as well as the resonance at δC 173.6 and 51.6, implying a ceramide structure for 1 (Table 1) (Balemaken et al., 2021). The characteristic resonances for the 2-amino-1,3,4-triol moiety were observed at δH 3.88 (dddd, *J* = 4.5, 5.5, 9.5, 10.0), H-2)/δC 51.6 (C-2), 3.55 (dd, *J* = 10.8, 5.2 Hz, H-1a) and 3.50 (dd, *J* = 10.8, 4.6 Hz, H-1b)/δC 60.9 (C-1), 3.36 (m, H-3)/δC 74.8 (C-3), and 3.33 (m, H-4)/δC 71.2 (C-4) (Balemaken et al., 2021; Tazoo et al., 2007). This was confirmed by correlations observed on its COSY 1H-1H (Fig. S7) spectrum, between protons: H-1a/H-1b and H-2, H-2 and H-3, H-3 and H-4, enabling the location of the three hydroxy groups. Moreover, the two primary methyl signals at δH 0.86 (6H, t, *J* = 6.5 Hz, H-22, 16')/δC 14.3 (C-22, 16') and the methylene groups cluster at δH 1.24-1.29/δc 29.1-30.0 ( δH 1.23-2.25/δC 22.5-33.6) associated to the two long chains strengthened the ceramide core structure of 1. This was further characterized by comparison of its NMR spectral data with those of related ceramide derivatives (Khedr et al., 2018; Balemaken et al., 2021). The NMR data of 1 were similar to those of previous reported rel-(2*S*,3*S*,4*R*,16*E*)-2-[(2'*R*)-2'-hydroxynonadecanoylamino]-heneicosadec-16-ene-1,3,4-triol isolated from *Acnistus arborescens* (Maia et al., 2010). The significant differences between 1 and the aforementioned compound, were the chain-lengths of the fatty acid (C16 in 1, while C19 for rel-(2*S*,3*S*,4*R*,16*E*)-2-[(2'*R*)2'-hydroxynonadecanoylamino]-heneicosadec-16-ene-1,3,4-triol) and sphingosine (C22 for 1, whereas C21 in rel-(2*S*,3*S*,4*R*,16*E*)-2-[(2'*R*)2'-hydroxynonadecanoylamino]-heneicosadec-16-ene-1,3,4-triol) moieties, as well as the location, number, and configuration of the double bonds (two double bonds with (E)-configurations on the sphingosine moiety in 1, while only one in rel-(2*S*,3*S*,4*R*,16*E*)-2-[(2'*R*)2'-hydroxynonadecanoylamino]-heneicosadec-16-ene-1,3,4-triol). In addition, the absence of an α-hydroxy substituent in fatty acid was noticeable. This finding was supported by the unequivocal HMBC correlations found between H-2' (δH 2.25) with C-1' (δC 173.6), C-3' (δC 28.7) and C-4' (δC 24.8). Positions of the hydroxy groups was also deduced from the HMBC spectrum in which the proton signal at δH 7.32 (N-H) showed correlations with the carbonyl (C-1') and the nitro-genated methine (C-2), while the proton signal at δH 3.88 (H-2) exhibited correlations with the carbons C-1 (δC 60.9), C-3 (δC 76.7), and C-4 (δC 71.2) respectively. Moreover, the extent of the long chain base (LCB) and the structure of the fatty acid were determined using HCl: MeOH mixture as described by Mohamed et al. (2015). The fatty acid methyl ester (FAME) resulting from that process was subjected to EI-MS analysis. The FAME spectrum residue was identified as methyl palmitate (C17H34O2) based on the GC and EI-MS analyses (Fig. S15) of the organic phase with a molecular ion peak at m/z 270 [M]+, confirmed by the positive ion peak at *m/z* 271 [M+H]+ in the LCMS spectrum. Accordingly, the molecular formula of the phytosphingosine unit had to be C24H49NO4. Taking into account the molecular mass of 1 (m/z 608 [M+H]+) and the characteristic LC-MS (APCI and UPLC) fragment ion peak at *m/z* 338, the LCB was assigned as (2*S*,3*S*,4*R*,10*E*,16*E*)- 2-aminodocos-10,16-diene-1,3,4-triol. The location of the double bond in the LCB was determined by the EI-MS analysis of the dimethyl disulfide (DMDS) derivative of 1 that showed remarkable fragment ion peaks at *m/z* 130 (C7H14S) and 212 (C13H24S) after cleavage of the double bond between the carbon atoms bearing each other a methylthio group (Fig. 3 and Fig. S17); hence, the double bonds in the LCB were located at C-10 and C-16 (Awouafack et al., 2018; Tsamo et al., 2021). These positions at C-10/C-11 and C-16/C-17 in the sphingosine moiety was also confirmed by fragmentation pattern occurring in EI-MS, through important allylic cleavages at *m/z* 71 [M-C33H62NO4]+, 97 [M-C33H60NO4]+, *m/z* 153 [M-C27H52NO4]+ and *m/z* 179 [M-C25H50NO4]+respectively (Fig. S19). The trans (E) configuration of the double bond was confirmed by the chemical shifts of the allylic carbons at δC 32.1 (C-9/C-12) and 32.9 (C-15/C-18) around the olefinic bonds (Rossi et al., 1982; Fusetani et al., 1989). The relative stereochemistry that might be inferred from the stereocenters C-2, C-3 and C-4 is *S*\*, *S*\* and *R*\* respectively, according to the close relationship between their chemical shifts (Table 1) with those of codonocerebroside A (δH 51.6 (C-2), 75.6 (C-3), 72.8 (C-4)) (Zhao et al., 2013). Additionally, a comparison with literature data of natural sphingamines (Dos Santos et al., 2012) led to the conclusion that the optical rotation of 1 ([α]D = + 9.27°) supported the (2*S*,3*S*,4*R*) configuration (Mohamed et al., 2013; Zhao et al., 2013; Tian et al., 2014). Thus, the structure of 1 was assigned as N-(2*S*\*, 3*S*\*, 4*R*\*, 10*E*, 16*E*)-1,3,4-trihydroxydocosa-10,16-dien-2-yl) palmitamide and named funtulaticamide.

Compounds 2-7 were identified as funtulatine (2) (Oletta, 1963), methyl ursolate (3) (Mukam et al., 1973), epicatechin (4) (Spek et al., 1984), myricetin (5) (Hinou et al., 1988), D-fructofuranosyl-β-(2 → 1)-α-D-glucopyranoside (sucrose) (6) (Yamamori et al., 2017).) and 5-hydroxypyridine-3-carboxamide (7) (Stolyarova et al., 1986) (Fig. 1) based on the comparison of their NMR data with the reported ones. Moreover, structure of compound 2, previously reported without clear specification of stereochemistry, was unambiguously assigned (Table S1) (see Fig. 4) (see Fig. 2).

***Table 1.***



***Figure 1****. Structures (1–7) of the isolated compounds from Funtumia elastica trunk bark.*



***Figure 2.*** *Selected 2D NMR correlations of 1.*



***Figure 3.*** *Possible fragmentation pattern of 1 (UPLC and EI).*



***Figure 4.*** *Mass Spectra fragmentation of methylthiolated alkenyl chains of ceramide*

1 (EI).



***Table 2.***



## In vitro antileishmanial activity

*Leishmania donovani* 1S (MHOM/SD/62/1S) promastigotes were cultivated at 28 °C in axenic M199 culture medium (Sigma Aldrich) supplemented with 10% heat-inactivated fetal bovine serum (FBS) (Sigma Aldrich) and 1% streptomycin/penicillin (Sigma Aldrich). The antileishmananial activity of test samples was determined as previously described (Siqueira-Neto et al., 2010) using the resazurin-based assay. Compounds were serially diluted in incomplete M199 medium and 10 μL of each compound were introduced in 90 μL of L. *donovani* promastigotes (4 × 105 parasites) from an exponential phase culture in complete medium. They were all screened at final concentrations of 100-0.16 μg/mL for extracts and fractions and 50-0.08 μg/mL for compounds and tests plates were incubated for 28 h at 28 °C, followed by the addition of 1 mg/mL resazurin. The negative and positive controls were 0.1% DMSO and amphotericin B (Sigma Darmstadt, Germany) (10-0.016 μg/mL), respectively. After an additional incubation of 44 h, plates were then read on a Magelan Infinite M200 fluorescence multi-well plate reader (Tecan) at an excitation and an emission wavelength of 530 and 590 nm, respectively. For each sample, growth percentages were calculated and dose-response curves were constructed to determine the 50% inhibitory concentration (IC50) using the GraphPad-version 5.0 software.

Biological assays against *L. donovani* were carried using plant crude extract and some isolates, according to a procedure already described in literature (Siqueira-Neto et al., 2010). Regarding the efficacy assay against Leishmania parasite, only compound 2 showed the best activity with an IC50 value 9.7 μg/mL (IC50 15.9 μM) whereas, 1 and 6 exhibited no significant biological activity with IC50 > 50.0 μg/mL (IC50 > 82.4 and 146.2 μM respectively). Interestingly, the highest antipromastigote activity was recorded for the extract (IC50 = 5.1 ± 0.9 μg/mL), suggesting that isolated constituents and unidentified compounds from the present study, might act synergistically to enhance the antilesimanial effect of the plant (Table 2).

## Data analysis

All the activity data represent mean ± standard deviation (SD) from three independent experiments. Microsoft Excel® software was used to calculate the percentages of inhibition. The IC50 and CC50 values were determined using Graph Pad prism 5.0 Software with data fitted by non-linear regression.

# Chemotaxonomic significance

Numerous alkaloids, flavonoids, triterpenoids, steroids and ceramides have previously been reported from genera within Apocynacae (Bhutani et al., 1990; Kawamoto et al., 2003; Liang et al., 2006; Hui et al., 2009; Patil et al., 2012; Jain et al., 2013; Zhao et al., 2014; Ebede et al., 2021, 2022), the structural diversity of these compounds across the genus Funtumia (including this study) has not yet been thoroughly investigated, it should be noted that its species are known to provide steroidal alkaloids, flavonoids and triterpenoids (Janot et al., 1960, 1963; Blanpin and Quevauviller, 1960; Oletta, 1963; Mukam et al., 1973; Wagner et al., 1987; Zirihi et al., 2005; Frempong et al., 2021a: 2021b; Kom et al., 2021) hence, these compounds might be of importance in chemotaxonomy.

**CRediT author contribution statement**

Larissa Kom: Conceptualization, Investigation, Methodology, Writing - original draft, Editing & formal analysis. Theodora Kopa: Writing - review & editing. Alembert Tchinda: Methodology, Writing - review, Editing & formal analysis. Auguste Abouem A Zintchem: Project administration & methodology. Dieudonne Emmanuel Pegnyemb: Coordinator, project administration & Methodology. Dominique Ngono Bikobo: Supervision, Methodology, Validation, Writing - review & editing. Michel Frédérich: Project administration, Funding acquisition, Supervision, Validation, Writing-review & editing.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bse.2022.104569>

# References

* Adekunle, A.A., Ikumapayi, A.M., 2006. Antifungal property and phytochemical screening of the crude extracts of Funtumia elastica and Mallotus oppositifolius. W. Indian Med. J. 55, 219–223.
* Awouafack, M.D., Tane, P., Morita, H., 2018. Tricalycoside, a new cerebroside from Tricalysia coriacea (Rubiaceae). Chem. Biodiversity 15 (1 of 6), e1700472. https://doi.org/10.1002/cbdv.201700472, 2018.
* Balemaken, M.M., Evina, J.N., Abouem, A.Z.A., October, N., Bona, A., Moela, P., Diboué, B.P.H., Ngono, B.D.S., Pegnyemb, D.E., 2021. Antibacterial and cytotoxic activities of undescribed cassiaric acid and other constituents from Cassia arereh stem barks. Nat. Prod. Res. https://doi.org/10.1080/14786419.2021.1981313.
* Betti, J.L., 2004. An ethnobotanical study of medicinal plants among the Baka pygmies in the Dja biosphere reserve, Cameroon. Afr. Stud. Monogr. 25, 1–27.
* Blanpin, O., Quevauviller, A., 1960. Comparative pharmacology of two alkaloids of steroid structure isolated from Funtumia latifolia, funtumine and funtumidine. An. Pharm. Fr. 18, 177–192.
* Blench, R., 2006. Archaeology, Language, and the African Past. AltaMira Press, Lanham, United States, p. 388 pp. ISBN. 978-0-7591-0466-2 (paperback).
* Bhutani, K.K., Vaid, R.M., Ali, M., Kapoor, R., Soodan, S.R., Kumar, D., 1990. Steroidal alkaloids from Holarrhena antidysenterica. Phytochemistry 29, 969–972.
* Burkill, H.M., 1995. The Useful Plants of West Tropical Africa, second ed. Royal Kew Botanical Gardens, London, pp. 522–527. 3:11.
* Dos Santos, E.O., Meira, M., do Vale, A.E., David, J.M., de Queir´oz, L.P., Juceni, P.D., 2012. Isolation and characterization of new ceramides from aerial parts of Lepidaploa Cotoneaster. Nat. Prod. Commun. 7, 781–783.
* Ebede, G.R., Ndongo, J.T., Mbing, J.N., Kenfack, H.C., Pegnyemb, D.E., Bochet, C.G., 2021. Contortamide, a new anti-colon cancer cerebroside and other constituents from Tabernaemontana contorta Stapf. (Apocynaceae). Nat. Prod. Res. 35, 1757–1765. https://doi.org/10.1080/14786419.2019.1636243.
* Ebede, G.R., Ngo Mbing, J., Nama, A.B., Shehla, N., Raman, A-U., Pegnyemb, D.E., Ndongo, J.T., Choudhary, M.I., 2022. New glycocerebrosides from the trunk of Tabernaemontana contorta Stapf. (Apocynaceae) and their antibacterial activity. Biochem. Syst. Ecol. 101, 104396. https://doi.org/10.1016/j.bse.2022.104396.
* Frempong, T.F., Badu, M., Boamah, V.E., Amponsah, I.K., Agbemade, B., Boateng, R.A., Boadi, N.O., 2021a. Phenolic content, antioxidant properties and antimicrobial activities of the extracts from Funtumia africana and Funtumia elastica. Chem. Africa 4, 503–512.
* Frempong, T.F., Boadi, N.O., Badu, M., 2021b. Optimization of extraction conditions for polyphenols from the stem bark of Funtumia elastica (Funtum) utilizing response surface methodology. AAS Open Res. 4, 46. https://doi.org/10.12688/aasopenres.13284.2.
* Fusetani, N., Yasumoto, K., Matsunaga, S., Hirota, H., 1989. Haliclamines A and B: cytotoxic macrocyclic alkaloids from a sponge of the genus Haliclona. Tetrahedron Lett. 30, 6891–6894.
* Hinou, J., Lakkas, N., Philianos, S., 1988. Les constituants polyph´enoliques de Myrtus communis L. Med. Plant. Phytother. 22, 98–103.
* Hui, T., Sun, Y., Zhu, L., Guo, W., Rao, G., 2009. Flavonoids in leaves of Alstonia scholaris. Zhongguo Zhong yao za zhi Zhongguo zhongyao zazhi. China J. Chin. Mater. Med. 34, 1111–1113.
* Ibrahim, S.R.M., Mohamed, G.A., Elkhayat, E.S., Gouda, Y.G., Proksch, P., 2008. Strepsiamide A-C, new ceramides from the marine sponge Strepsichordaia lendenfeldi. Nat. Prod. Commun. 3, 205–209.
* Jain, S., Sharma, P., Ghule, S., Jain, A., Jain, N., 2013. In vivo anti-inflammatory activity of Tabernaemontana divaricata leaf extract on male albino mice. Chin. J. Nat. Med. 11, 472–476.
* Janot, M.M., Cav´e, A., Goutarel, R., 1960. Bulletin de la Soci´et´e Chimique de France 3, compte rendu, pp. 251–559.
* Janot, M.M., Truong-Ho, M., Khuong-Huu, Q., Goutarel, R., 1963. Bull. Soc. Chim. Fr. 3, 1977.
* Kawamoto, S., Koyano, T., Kowithayakorn, T., Fujimoto, H., Okuyama, E., Hayashi, M., Komiyama, K., Ishibashi, M., 2003. Wrightiamines A and B, two new cytotoxic pregnane alkaloids from Wrightia javanica. Chem. Pharm. Bull. 51, 737–739.
* Khedr, A.I.M., Ibrahim, S.R.M., Mohamed, G.A., Yamada, K., Ross, S.A., 2018. Panduramides A-D, new ceramides from Ficus pandurata fruits. Phytochem. Lett. 23, 100–105.
* Kom, M.L., Abouem, A.Z.A., Kopa, K.T., Atchad´e, A.T., Tchokouaha, Y.L., Fr´ed´erich, M., Ngono, B.D.S., Pegnyemb, D.E., 2021. Antiplasmodial and antileishmanial inhibitory activity of triterpenes and steroidal alkaloid from the leaves of Funtumia elastica (Preuss) Stapf (Apocynaceae). Fitoterapia 151, 104869. https://doi.org/10.1016/j.fitote.2021.104869.
* Liang, S., Chen, H.S., Du, J.L., Wang, H.P., Shen, Y., Huang, M.Z., 2006. Study on chemical constituents of Tabernaemontana divaricata. Acad. J. Second Mil. Med. Univ. 27, 892–894.
* Maia, A.I.V., Veras, M.L., Braz-Filho, R., Lopes, N.P., Silveira, E.R., Pessoa, O.D.L., 2010. New ceramides from Acnistus arborescens. J. Braz. Chem. Soc. 21, 867–871.
* Mohamed, G.A., Ibrahim, S.R.M., Elkhayat, E.S., Ross, S.A., Sayed, H.M., El-Moghazy, S.A.M., El-Shanawany, M.A., 2015. Blepharisides A and B: new flavonol glycosides from Blepharis ciliaris growing in Saudi Arabia. Phytochem. Lett. 11, 177–182.
* Mohamed, G.A., Ibrahim, S.R.M., Ross, S.A., 2013. New ceramides and isoflavone from the Egyptian Iris germanica L. rhizomes. Phytochem. Lett. 6, 340–344.
* Mukam, L., Charles, G., Hentchoya, J., Njimi, T., Ourisson, G., 1973. Le cyclofuntumienol, methyl-4α sterol en C 31 de Funtumia elastica, France. Tetrahedron Lett. 29, 2779–2782.
* Odugbemi, T., 2006. Outlines and Pictures of Medicinal Plants from Nigeria. University of Lagos Press, Unilag, p. 158.
* Olaniyi, A.A., 1989. Essential Medicinal Chemistry, fourth ed. Shaneson C I Ltd, Ibadan, Nigeria, pp. 474–475.
* Oletta, S.A., 1963. An alkaloid obtained from the bark of Funtumia latifolia, 1,328,589 in Chem. Abstr. (1964). French Patent 60, 642.
* Patil, R.P., Pai, S.R., Pawar, N.V., Shimpale, V.B., Patil, R.M., Nimbalkar, M.S., 2012. Chemical characterization, mineral analysis, and antioxidant potential of two underutilized berries (Carissa carandus and Eleagnus conferta) from the Western Ghats of India. Crit. Rev. Food Sci. Nutr. 52, 312–320.
* Rossi, R., Carpita, A., Quirici, M.G., Veracini, C.A., 1982. Insect pheromone components: use of 13C NMR spectroscopy for assigning the configuration of C–C double bonds of monoenic or dienic pheromone components and for quantitative determination of Z/E mixtures. Tetrahedron 38, 639–644.
* Siqueira-Neto, J.L., Song, O.R., Oh, H., Sohn, J.H., Yang, G., Nam, J., Jang, J., Cechetto, J., Lee, C.B., Moon, S., Genovesio, A., Chatelain, E., Christophe, T., Freitas-Junior, L.H., 2010. Antileishmanial high-throughput drug screening reveals drug candidates with new scaffolds. PLoS Neglected Trop. Dis. 4, 675. https://doi.org/10.1371/journal.pntd.0000675.
* Spek, K.P., Koji´c-Prodi´c, B., Labadie, R.P., 1984. Structure of (-)-epicatechin: (2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-1-benzopyran-3,5,7-triol, C15H14O6. Acta Crystallogr. Sect. C Cryst. Struct. Commun. 40, 2068–2071.
* Stolyarova, L.G., Akhundov, R.A., Rakhmankulova, I.K., Voronina, T.A., Smimov, L.D., Dyamaev, K.M., 1986. Synthesis and psychopharmacological and antihypoxic activity of some β-substituted pyridine carboxylic acids. Pharm. Chem. J. 20, 29–31.
* Tazoo, D., Krohn, K., Hussain, H., Kouam, S.F., Dongo, E., 2007. Laportoside A and Laportomide A: a new cerebroside and a new ceramide from leaves of Laportea ovalifolia. Z. Naturforsch. 62b, 1208–1212.
* Tian, X.R., Tang, H.F., Feng, J.T., Li, Y.S., Lin, H.W., Fan, X.P., Zing, X., 2014. Neritinaceramides A–E, New ceramides from the marine bryozoan Bugula neritina inhabiting South China sea and their cytotoxicity. Mar. Drugs 72, 1987–2003.
* Tolela, M.D.L., Foche, P., 1979. Minor alkaloids of the seeds of Funtumia elastica of Zaire. Planta Med. 35, 48–50.
* Tsamo, L.D.F., Yimgang, L.V., Wouamba, S.C.N., Mkounga, P., Nkengfack, A.E., Voutquenne-Nazabadioko, L., Ngnokam, D., Ndjakou Lenta, B., Sewald, N., 2021. A New ceramide (tumexamide) and other chemical constituents from Rumex abyssinicus Jacq (Polygonaceae): isolation, characterization, antibacterial activities and chemophenetic Significance. Adv. Biol. Chem. 11, 266–282.
* Truong-Ho, M., Khuong-Huu, Q., Goutarel, R., 1963. Alcaloïdes st´eroïdiques XV. Les irehdiamines A et B, alcaloïdes du Funtumia elastica (Preuss) Stapf. Bull. Soc. Chim. France 594.
* Wagner, H., Seegert, K., Sonnenbichler, H., Ilyas, M., Odenthal, K.P., 1987. Steroid alkaloids of Funtumia africana. Planta Med. 53, 444–449.
* Yamamori, A., Takata, Y., Fukushi, E., Kawabata, J., Okada, H., Kawazoe, N., Ueno, K., Onodera, S., Shiomi, N., 2017. Strutural analysis of novel low-digestible sucrose Isomers synthesized from D-glucose and D-fructose by thermal treatment. J. Appl. Glycosci. 64, 15–19.
* Zhao, B., Gang, X.H., Yuan, Z., 2013. Isolation of a new cerebroside from Codonopsis lanceolata. Biochem. Systemat. Ecol. 46, 23–28.
* Zhao, C., Ren, J., Gong, X.J., Chen, H.G., Zhou, X., 2014. Ceramides of Periploca forrestii. Chin. J. Exp. Tradit. Med. 20, 83–85.
* Zirihi, G.N., Grellier, P., Gu´ed´e-Guina, F., Bodo, B., Mambu, L., 2005. Isolation, characterization and antiplasmodial activity of steroidal alkaloids from Funtumia elastica (Preuss) Stapf. Bioorg. Med. Chem. Lett. 15, 2637–2640.