OPEN ACCESS Freely available online
www.banglajol.info/index.php/JSF
Journal of Science Foundation
January 2020, Vol. 18, No. 1, pp. 13-18
ISSN (Print) 1728-7855
DOI: https://doi.org/10.3329/jsf.v18i1.51278

Original Article

Triterpenoids Isolated from Stem Bark of Glochidion lanceolarium (Roxb.), Voigt

Selina Kabir[1], Mohammad Rashedul Haque[2], Abdullah Mohammad Sarwaruddin Chowdhury[3], Mohammad Abdur Rashid[4], Choudhury Mahmood Hasan[5]

Abstract

This paper presents the chemical investigation of the stem barks of *Glochidion lanceolarium* (Roxb.) Voigt, Euphorbiaceae. Classic phytochemical investigation of organic extracts of the aerial parts of *Glochidion lanceolarium* together with spectroscopic methods led to the isolation and characterization of three triterpenes, namely Epilupeol (1) Glochidonol (2), Glochidone (3). [*Journal of Science Foundation, January 2020;18(1):13-18*]

Keywords: Triterpenes; Epilupeol; Glochidonol; Glochidone; *Phyllanthus*; *Glochidion*

*[**Reviewed:** 3 November 2019; **Accepted on:** 1 December 2019; **Published on:** 1 January 2020]*

Introduction

Glochidion was regarded as a genus of the family Euphorbiaceae, which consists of monoecious, rarely dioecious trees or shrubs. But molecular phylogenetic studies have shown that Phyllanthus is paraphyletic over Glochidion. A recent revision of the family Phyllanthaceae has subsumed Glochidion into Phyllanthus (Hoffmann et al., 2006). Glochidion lanceolarium (Roxb.) Voigt, locally known as Kechchua, Bhauri, Kakra, Anguti is a small to medium-sized evergreen tree usually 1-3m tall, rarely 7-12 m tall. The plant grows in Chittagong, Cox's Bazaar and Sylhet of Bangladesh. It is also available in Bhutan, India, Myanmar and Nepal (Rahman, 2008).

Traditionally many *Phyllanthus* species are used in haemorrhoids, diarrhoea, dysentery, anaemia, jaundice, dyspepsia, insomnia etc. and some of them can induce diuresis (Ghani, 1998). In Chinese traditional medicine *Glochidion puberum* is used in dysentery, jaundice, leukorrhagia, common cold, sore throat, toothache, carbuncle, furuncle, rheumatic arthralgia (Fenglin et al., 2004). Recent investigation showed that *Glochidion multilculare* possess antitumor, analgesic and anti-inflamatory potential (Kabir et al., 2015).

[1]Department of Applied Chemistry & Chemical Engineering, University of Dhaka, Dhaka, Bangladesh
[2]Department of Pharmaceutical Chemistry, University of Dhaka, Dhaka, Bangladesh
[3]Department of Applied Chemistry & Chemical Engineering, University of Dhaka, Dhaka, Bangladesh
[4]Department of Pharmaceutical Chemistry, University of Dhaka, Dhaka, Bangladesh
[5]Department of Pharmaceutical Chemistry, University of Dhaka, Dhaka, Bangladesh

Correspondence: Selina Kabir, Department of Applied Chemistry & Chemical Engineering, University of Dhaka, Bangladesh; **Email:** selinakabir.bd@gmail.com

Biological investigations of *Phyllanthus* species revealed that many members of the genus possess anti-tumor promoting ability (Huang et al., 2006; Rajeshkumar et al., 2002; Tanaka et al., 2004), apoptosis inducing ability (Huang et al., 2004; Puapairoj et al., 2005), antiviral activity against hepatitis B virus (Lam et al., 2006; Venkateswaran et al., 1987), anti-angiogenic effect (Huang et al., 2006), analgesic effect (Santos et al., 1994, 2000), diuretic effect (Srividya and Periwal, 1995), lipid lowering activity (Khanna et al., 2002), hypocholesterolemic activity (Adeneye et al., 2006), antioxidative effect (Harish and Shivanandappa, 2006; Raphael et al., 2002; Sabir and Rocha, 2008), antidiabetic effect (Adeneye et al., 2006; Raphael et al., 2002; Srividya and Periwal, 1995), antiherpetic activity (Álvarez et al., 2009; Yang et al., 2007), hepatoprotective effect (Harish and Shivanandappa, 2006; Sabir and Rocha, 2008), anti-inflammatory action (Kassuya et al., 2006; Kiemer et al., 2003), antiatherogenic effect (Duan et al., 2005), anti-HIV activity (Notka et al., 2003, 2004; Ogata et al., 1992); antiplasmodial activity (Luyindula et al., 2004), antibacterial activity (Meléndez and Capriles, 2006), hypotensive activity (Leeya et al., 2010; Srividya and Periwal, 1995).

Many secondary metabolites were isolated from *Glochidion* species, including tannins (Chen et al., 1995), glycosides (Otsuka et al., 2003), lignans (Otsuka et al., 2000), terpenoids (Hui and Li, 1976). Glochidiol, glochilocudiol, glochidone and dimedone were isolated from *G. multiloculare* (Talapatra *et al.*, 1973). Previous phytochemical investigations of *G. lanceolarium* led to the isolation of triterpenes 3-epilupeol, glochidone and glochidiol from the bark and roots (Asolkar *et al*., 1992). We describe here the chemical characterization of triterpenes obtained from *G. lanceolarium* along with a small review regarding the importance of these compounds.

Methodology

General experimental procedures: Mass measurements were conducted on a Micromass Q-TOF Ultima Gloval Tandem mass spectrometer. 1H- and 13C- NMR spectra were acquired with a Bruker AMX–500 (500 MHz for ^{1}H and 100 MHz for ^{13}C) spectrometer and the spectra were referenced to the residual non-deuterated solvent signals. *J*-modulated ^{13}C spectra were acquired with a relaxation time (d1) of 4 s. Vacuum liquid chromatography (VLC) was done over silica gel (Kieselgel 60H, mesh 70-230, Merck). while TLC and preparative TLC (pTLC) were performed by using silica gel 60 PF254 on glass plates (5 × 20 and 20 × 20 cm, thickness 0.5 mm) and the compounds were visualized under UV light (254 and 366 nm) and by spraying the developed plates with vanillin-sulfuric acid, followed by heating at 110^{o}C for 5-10 mins.

Plant material: The stem bark of *G. lanceolarium* was collected from Mirpur, Dhaka in the month of April, 2009 and identified by Mr. Sarder Nasir Uddin, Scientific Officer, Bangladesh National Herbarium, Dhaka, where a voucher specimen (DACB-34199) representing this collection has been deposited. Stem bark of this plant was air-dried for several days followed by oven-drying for 24 hours and then ground to a coarse powder.

Extraction and Isolation: The air dried powdered plant material (900 g) was successively cold extracted with methanol (7 days) at room temperature with occasional shaking and stiring. The extractives were filtered through fresh cotton plug and followed by whatman no. 1 filter paper. The filtrate were then concentrated by a Buchii rotavapor at low temperature and pressure and afforded methanol (MEGL) extract (36.8199g). The cold methanol extract (10 g) was subjected to Solvent-Solvent partitioning using the protocol designed by Kupchan and modified by Wagene (Vanwagenen *et al*., 1993). The extract was partioned successively with petroleum ether, carbon tetrachloride and chloroform. Evaporation of solvents afforded petroleum ether (PEFGL, 3.5 g), carbon tetrachloride (CTFGL, 2.6 g), chloroform (CFFGL, 700 mg) and aqueous (AQFGL, 1.9 g). A portion of the carbon tetrachloride soluble fraction (1 g) was subjected to Vacuum Liquid Chromatography (VLC) for fractionation. The column was filled with fine TLC grade silica gel (kieselgel 60H, mesh 70-230) and eluted with petroleum ether, followed by petroleum ether and ethyl acetate mixtures of increasing polarities and finally with ethyl acetate and methanol in order of increasing polarities. A total of 28 fractions were collected. The VLC fractions 5A and 5B were combined together on the basis of TLC analysis. Preparative TLC of the VLC fractions developed with 5% EtOAc in tolune afforded compound **1 (**2.5 mg). Depending on the TLC behavior, fractions 6B and 7A were bulked together and Preparative Thin Layer Chromatography (PTLC) developed with 10% EtOAc in tolune afforded compound **2 (**3.5 mg). The

VLC fractions 9B and 10(A+B) were mixed together on the basis of the similar TLC feature and subjected to Preparative Thin Layer Chromatography PTLC with 12% EtOAc in toluene yielded compound **3 (**5mg).

Results and Discussion

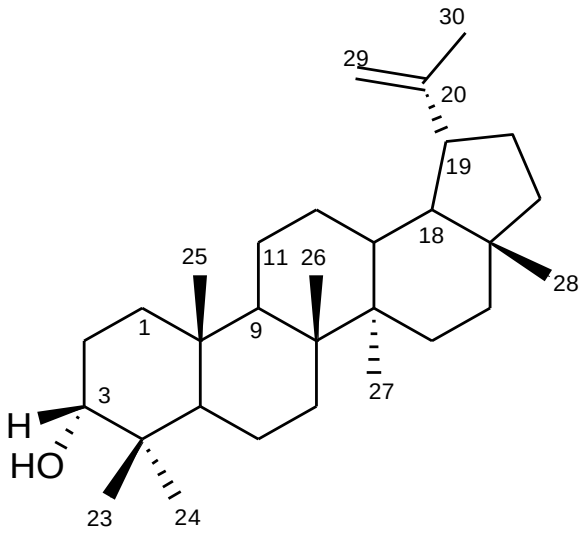

Figure I: Structure of Epilupeol

Epilupeol (I): white crystals; *ESI-MS*: *m/z* 427 $[M + H]^+$ ($C_{30}H_{50}O$, M = 426); ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.39 (1H, t, H-3), 2.39 (1H, ddd, *J* = 11.2, 11.2, 6.0 Hz, H-19), 0.83 (3H, s, H-23), 0.94 (3H, s, H-24), 0.85 (3H, s, H-25), 1.04 (3H, s, H-26), 0.96 (3H, s, H-27), 0.79 (3H, s, H-28), 4.69 (1H, d, *J* = 2.4 Hz, H_a-29), 4.57 (1H, dd, 2.4, *J* = 2.4, 1.6, H_b- 29), 1.68 (3H, s, H-30); ^{13}C NMR (100 MHz, $CDCl_3$) : δ (ppm) 33.2 (C-1), 25.4 (C-2), 76.2 (C-3), 38.0 (C-4), 49.7 (C-5), 18.3 (C-6), 34.1 (C-7), 40.0 (C-8), 50.2 (C-9), 38.0 (C-10), 19.2 (C-11), 25.1 (C-12), 38.0 (C-13), 43.0 (C-14), 27.4 (C-15), 35.6 (C-16) 42.9 (C-17), 49.0 (C-18), 49.0 (C-19), 150.9 (C-20), 28.2 (C-21), 40.0 (C-22), 27.4 (C-23), 22.1 (C-24), 15.9 (C-25), 15.9 (C-26), 14.6 (C-27), 18.0 (C-28), 109.2 (C-29), 19.3 (C-30)

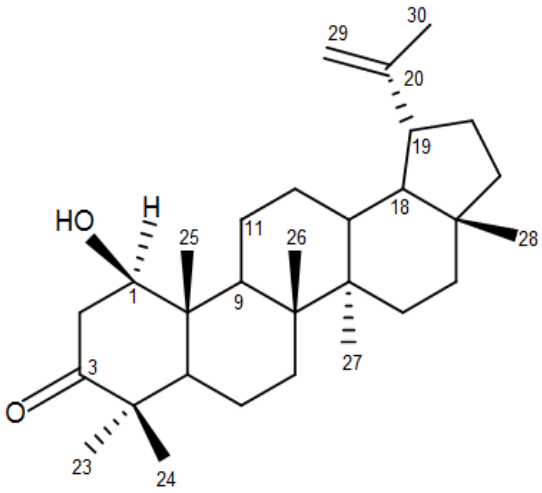

Figure II: Structure of Glochidonol

Glochidonol (II): white crystal, *ESI-MS*: *m/z* 441$[M + H]^+$ ($C_{30}H_{48}O_2$, M = 440); ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.89 (1H, dd, *J* = 8.0, 3.6, H_{α},-1), 2.99 (1H, dd, *J*=14.4, 8.0, H_{ax}-2), 2.21 (1H, dd, *J*=14.4, 3.6, Heq -2), 2.38 (1H, dt, *J*= 11.2, 5.6, H-19), 4.69 (1H, d, *J*= 2.0, H_a-29), 4.57 (1H, br. S, H_b-29), 1.06 (3H, s, H-23), 1.04 (3H, s, H-24), 0.84 (3H, s, H-25), 1.06 (3H, s, H-26), 0.98 (3H, s, H-27), 0.80 (3H, s, H-28), 1.68 (3H, s, H-30)

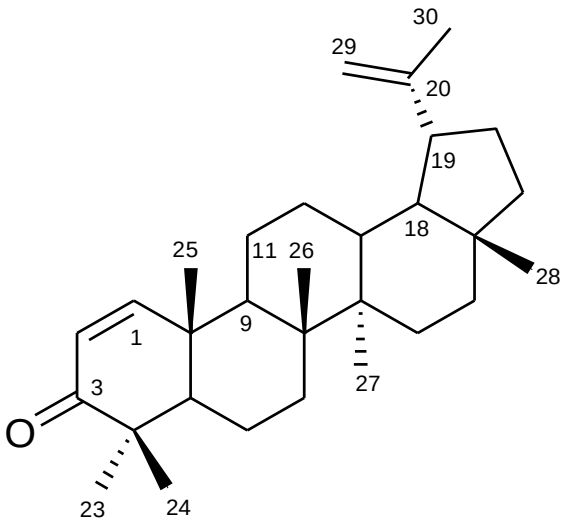

Figure III: Structure of Glochidone

Glochidone (III): Oily substance, *ESI-MS*: *m/z* 422.69 $[M + H]^+$, ($C_{30}H_{46}O$); ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.10 (1H, d, *J* =10.0, H-1), 5.79 (1H, d, *J* =10.0, H-2), 2.40 (1H, dt, *J* =11.0, 6.0, H-19), 4.71 (1H, d, *J* =2.0, H_a -29), 4.59 (1H, m, H_b -29), 1.07 (3H, s, H-23), 1.08 (3H, s, H-24), 1.13 (3H, s, H-25), 1.12 (3H, s, H-26), 0.96 (3H, s, H-27), 0.81 (3H, s, H-28), 1.69 (3H, s, H-30)

Compound I was isolated as white crystal from the carbon tetrachloride soluble fraction of the stem bark of *G. lanceolarium*. The high-resolution ESI mass spectrum of Compound 1 showed the pseudo-molecular ion peak, $[M + H]^+$ at *m/z*, 427 which was consistent with a molecular formula ($C_{30}H_{50}O$, M = 426) for this compound. The ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum revealed typical signals for 50 protons and 30 carbons including seven tertiary methyls, one oximethine and one terminal di-substituted double bond (Thu et al., 2010).

The ^1H NMR spectrum (500 MHz, $CDCl_3$) of compound 1 showed a trplet (*J* =2.8) of one proton intensity at δ 3.39 typical for an oxymethine proton at C-3 of a triterpene type carbon skeleton. The absence of a double doublet and the appearance of a triplet suggested that the hydroxy group was at the α (alpha)-position, thus confirming the β (beta) orientation of C-3 proton (Alam et al., 2009). The spectrum displayed a doublet at δ 4.69 (*J*=2.4) and a double doublet at δ 4.57 (2.4, 1.6) assignable to the vinylic protons at C-29. Triple doublet at δ 2.39 (11.2, 11.2, 6.0) could be ascribed to proton at C-19. The spectrum also displayed seven singlets at δ 0.83, 0.94, 0.85, 1.04, 0.96, 0.79 and 1.68 (3H each) for methyl protons at C-4 (H_3-23, H_3-24), C-10 (H_3-25), C-8 (H_3-26), C-14 (H_3-27), C-17 (H_3-28) and C-20 (H_3-30), respectively. On this basis and by comparing these ^1H NMR and ^{13}C NMR data with literature values (Thu et al., 2010; Alam et al., 2009), compound 1 was identified as epilupeol. The identity of compound 1 was further substantiated by co-TLC with an authentic sample. This is the first report of this compound from *G. lanceolarium.*

Compound II was isolated as white crystal from the carbon tetrachloride soluble fraction of the stem bark of *G. lanceolarium* The high-resolation ESI mass spectrum of Compound II showed the pseudo-molecular ion peak, $[M + H]^+$ at *m/z*, 441 which was consistent with a molecular formula ($C_{30}H_{48}O_2$, M = 440) for this compound (Thu *et al.*, 2010). The ^1H NMR ($CDCl_3$, 500 MHz) spectrum of Compound **2** displayed methyl group resonances at δ 1.06, 1.04, 0.84, 1.06, 0.98, 0.80 and 1.68 were attributed to H_3-23, H_3-24, H_3-25, H_3-26, H_3-27, H_3-28 and H_3-30 respectively. The spectrum showed a doublet at δ 4.69 (2.0) and a singlet at 4.57 assignable to protons at C-29. A doublet of triplets at δ 2.38, (11.2, 6.0) integrating one proton intensity is indicative of H-19. A double doublets at δ 3.89 (8.0, 3.6) integrating one proton, is indicative of Hα-1. Two doublets of doublets at δ 2.99 (14.4, 8.0) and δ 2.21 (14.4, 3.6) are assignable to H_{ax}-2 and H_{eq}-2 respectively. On this basis and by comparing these ^1H NMR data with literature values (Hui et al., 1976; Thu et al., 2010), compound II was identified as glochidonol. The identity of Compound **2** was further substantiated by co-TLC with an authentic sample. This is the first report of this compound from *G. lanceolarium*.

Compound III was isolated as oily substance from carbon tetrachloride soluble fraction of the stem bark of *G. lanceolarium*. The high-resolation ESI mass spectrum of Compound III showed the pseudo-molecular ion peak at *m/z* 422.69 which was consistent with a molecular formula, $C_{30}H_{46}O$ for this compound. The ^1H NMR ($CDCl_3$, 500 MHz) spectrum of Compound III showed a doublet at δ 7.10, integrating for one proton, is indicative of H-1. A doublet at δ 5.79, d (10.0) was assigned to H-2. A doublet of triplets at δ 2.40, dt (11.0, 6.0), integrating one proton was indicative of H-19. The spectrum exhibited two doublets at δ 4.71, d (2.0) and 4.59, m was assigned to protons at C-29. The spectrum also displayed seven singlets at δ 1.07, 1.08, 1.13, 1.12, 0.96, 0.81 and 1.69 (3H each) for methyl protons at C-4 (H_3-23, H_3-24), C-10 (H_3-25), C-8 (H_3-26), C-14 (H_3-27), C-17 (H_3-28) and C-20 (H_3-30), respectively. These spectral features are in close agreement to those observed for glochidone (Hui et al., 1976; Neto et al., 1995). This is the first report of this compound from this plant.

Glochidonol and glochidiol show strong antiproliferative activity against three human tumor cell lines, MCF-7, NCI-H-460 and SF-268, through the involvement of apoptosis (Puapairoj et al., 2005). Glochidone shows pronounced antinociceptive properties in mice (Krogh et al., 1999). Lupeol is reported to exhibit a spectrum of pharmacological activities against various disease conditions such as inflammation, arthritis, diabetes, cardiovascular ailments, renal disorder, hepatic toxicity, microbial infections and cancer (Saleem, 2009; Siddique and Saleem, 2011).

Conclusion

In conclusion Glochidonol and glochidiol show strong anti-proliferative activity against three human tumor cell lines, MCF-7, NCI-H-460 and SF-268, through the involvement of apoptosis.

***Conflict of interest statement**: We declare that we have no conflict of interest.*

***Acknowledgements:** The authors are thankful to the Department of Pharmaceutical Chemistry, University of Dhaka, and Department of Applied Chemistry & Chemical Engineering, University of Dhaka, Bangladesh for providing laboratory facilities to carry out this research work. The Bose Centre for Advanced Study and Research in Natural Sciences, University of Dhaka, Bangladesh is gratefully acknowledged for partial financial support to carry out the research work.*

References

Adeneye AA, Amole OO, Adeneye AK. Hypoglycemic and hypocholesterolemic activities of the aqueous leaf and seed extract of Phyllanthus amarus in mice. Fitoterapia. 2006;77(7-8):511-4

Alam F, Rahman MS, Alam MS, Hossain MK, Hossain MA, Rashid MA. Phytochemical and Biological investigations of Phoenix paludosa Roxb. Dhaka University Journal of Pharmaceutical Sciences. 2009;8(1):7-10

Alvarez AL, del Barrio G, Kourí V, Martínez PA, Suárez B, Parra F. In vitro anti-herpetic activity of an aqueous extract from the plant Phyllanthus orbicularis. Phytomedicine. 2009;16(10):960-6

Asolkar LV, Kakkar KK, Chakre OJ. Second supplement to glossary of Indian medicinal plants with active principles part-I (AK). Council of scientific and industrial research (PID)(part-I), New Delhi. 1992:217-8

Chen LG, Yang LL, Yen KY, Hatano T, Yoshida T, Okuda T. Tannins of euphorbiaceous plants. XIII. New hydrolyzable tannins having phloroglucinol residue from glochidion rubrum BLUME. Chemical and pharmaceutical bulletin. 1995;43(12):2088-90

Duan W, Yu Y, Zhang L. Antiatherogenic effects of phyllanthus emblica associated with corilagin and its analogue. Yakugaku Zasshi. 2005;125(7):587-91

Fenglin H, Ruili L, Liang M. Free radical scavenging activity of extracts prepared from fresh leaves of selected Chinese medicinal plants. Fitoterapia. 2004;75(1):14-23

Ghani A. Medicinal plants of Bangladesh: chemical constituents and uses. Asiatic society of Bangladesh; 1998;260-262

Harish R, Shivanandappa T. Antioxidant activity and hepatoprotective potential of Phyllanthus niruri. Food chemistry. 2006;95(2):180-5

Hoffmann P, Kathriarachchi H, Wurdack KJ. A phylogenetic classification of Phyllanthaceae (Malpighiales; Euphorbiaceae sensu lato). Kew Bulletin. 2006:37-53

Huang ST, Yang RC, Lee PN, Yang SH, Liao SK, Chen TY, Pang JH. Anti-tumor and anti-angiogenic effects of Phyllanthus urinaria in mice bearing Lewis lung carcinoma. International immunopharmacology. 2006;6(6):870-9

Huang ST, Yang RC, Pang JH. Aqueous extract of Phyllanthus urinaria induces apoptosis in human cancer cells. The American Journal of Chinese Medicine. 2004;32(02):175-83

Hui WH, Li MM. Lupene triterpenoids from Glochidion eriocarpum. Phytochemistry. 1976;**15**: 561-562

Kabir S, Zahan R, Chowdhury AM, Haque MR, Rashid MA. Antitumor, analgesic and anti-inflammatory activities of Glochidion multiloculare (Rottler ex Willd) Voigt. Bangladesh Pharmaceutical Journal. 2015;18(2):142-8

Kassuya CA, Silvestre A, Menezes-de-Lima Jr O, Marotta DM, Rehder VL, Calixto JB. Antiinflammatory and antiallodynic actions of the lignan niranthin isolated from Phyllanthus amarus: evidence for interaction with platelet activating factor receptor. European Journal of Pharmacology. 2006;546(1-3):182-8

Kiemer AK, Hartung T, Huber C, Vollmar AM. Phyllanthus amarus has anti-inflammatory potential by inhibition of iNOS, COX-2, and cytokines via the NF-κB pathway. Journal of Hepatology. 2003;38(3):289-97

Khanna AK, Rizvi F, Chander R. Lipid lowering activity of Phyllanthus niruri in hyperlipemic rats. Journal of ethnopharmacology. 2002;82(1):19-22

Krogh R, Kroth R, Berti C, Madeira AO, Souza MM, Cechinel-Filho V, Delle-Monache F, Yunes RA. Isolation and identification of compounds with antinociceptive action from Ipomoea pes-caprae (L.) R. Br. Die pharmazie. 1999;54(6):464

Lam WY, Leung KT, Law PT, Lee SM, Chan HL, Fung KP, Ooi VE, Waye MM. Antiviral effect of Phyllanthus nanus ethanolic extract against hepatitis B virus (HBV) by expression microarray analysis. Journal of cellular biochemistry. 2006;97(4):795-812

Leeya Y, Mulvany MJ, Queiroz EF, Marston A, Hostettmann K, Jansakul C. Hypotensive activity of an n-butanol extract and their purified compounds from leaves of Phyllanthus acidus (L.) Skeels in rats. European journal of pharmacology. 2010;649(1-3):301-13

Luyindula N, Tona L, Lunkebila S, Tsakala M, Mesia K, Musuamba CT, et al. In vitro antiplasmodial activity of callus culture extracts from fresh apical stems of Phyllanthus niruri: Part 1. Pharmaceutical biology. 2004;42(7):512-8

Meléndez PA, Capriles VA. Antibacterial properties of tropical plants from Puerto Rico. Phytomedicine. 2006;13(4):272-6

Neto JO, Agostinho SM, Da Silva MF, Vieira PC, Fernandes JB, Pinheiro AL, Vilela EF. Limonoids from seeds of Toona ciliata and their chemosystematic significance. Phytochemistry. 1995;38(2):397-401

Notka F, Meier G, Wagner R. Concerted inhibitory activities of Phyllanthus amarus on HIV replication in vitro and ex vivo. Antiviral research. 2004;64(2):93-102

Notka F, Meier GR, Wagner R. Inhibition of wild-type human immunodeficiency virus and reverse transcriptase inhibitor-resistant variants by Phyllanthus amarus. Antiviral research. 2003;58(2):175-86

Ogata T, Higuchi H, MOCHIDA S, MATSUMOTO H, KATO A, ENDO T, KAJI A, KAJI H. HIV-1 reverse transcriptase inhibitor from Phyllanthus niruri. AIDS research and human retroviruses. 1992;8(11):1937-44

Otsuka H, Kijima H, Hirata E, Shinzato T, Takushi A, Bando M, Takeda Y. Glochidionionosides A—D: Megastigmane Glucosides from Leaves of Glochidion zeylanicum (G AERTN.) A. J USS. Chemical and pharmaceutical bulletin. 2003;51(3):286-90

Puapairoj P, Naengchomnong W, Kijjoa A, Pinto MM, Pedro M, Nascimento MS, et al. Cytotoxic activity of lupane-type triterpenes from Glochidion sphaerogynum and Glochidion eriocarpum two of which induce apoptosis. Planta medica. 2005;71(03):208-13

Rahman MO. *Glochidion lanceolarium*. In: Ahmed ZU, Hassan MA, Begum ZNT, Khondker M, Kabir SMH, Ahmad M, Ahmed ATA, Rahman AKA and Haque EU (eds.). Encyclopedia of flora and fauna of Bangladesh, Vol.**7**. Angiosperms: Dicotyledons (Balsaminaceae - Euphorbiaceae). Asiatic Society of Bangladesh, Dhaka. 2008;439-440

Rajeshkumar NV, Joy KL, Kuttan G, Ramsewak RS, Nair MG, Kuttan R. Antitumour and anticarcinogenic activity of Phyllanthus amarus extract. Journal of Ethnopharmacology. 2002;81(1):17-22

Raphael KR, Sabu MC, Kuttan R. Hypoglycemic effect of methanol extract of Phyllanthus amarus Schum & Thonn on alloxan induced diabetes mellitus in rats and its relation with antioxidant potential. Indian J Exp Biol, 2002;40:905-909

Sabir SM, Rocha JB. Water-extractable phytochemicals from Phyllanthus niruri exhibit distinct in vitro antioxidant and in vivo hepatoprotective activity against paracetamol-induced liver damage in mice. Food Chemistry. 2008;111(4):845-51

Saleem M. Lupeol, a novel anti-inflammatory and anti-cancer dietary triterpene. Cancer letters. 2009 Nov 28;285(2):109-15

Santos AR, De Campos RO, Miguel OG, Cechinel Filho V, Siani AC, Yunes RA, Calixto JB. Antinociceptive properties of extracts of new species of plants of the genus Phyllanthus (Euphorbiaceae). Journal of Ethnopharmacology. 2000;72(1-2):229-38

Santos AR, Filho VC, Niero R, Viana AM, Moreno FN, Campos MM, Yunes RA, Calixto JB. Analgesic effects of callus culture extracts from selected species of Phyllanthus in mice. Journal of Pharmacy and Pharmacology. 1994;46(9):755-9

Siddique HR, Saleem M. Beneficial health effects of lupeol triterpene: a review of preclinical studies. Life sciences. 2011;88(7-8):285-93

Srividya NA, Periwal S. Diuretic, hypotensive and hypoglycaemic effect of Phyllanthus amarus. Indian Journal of Experimental Biology. 1995;33(11):861-4

Talapatra SK, Bhattacharya S, Maiti BC, Talapatra B. Structure of glochilocudiol: a new triterpenoid from Glochidion multiloculare: natural occurrence of dimedone. Chem Ind Lond. 1973;21:1033-1034

Tanaka R, Kinouchi Y, Wada SI, Tokuda H. Potential anti-tumor promoting activity of lupane-type triterpenoids from the stem bark of Glochidion zeylanicum and Phyllanthus flexuosus. Planta medica. 2004;70(12):1234-6

Thu VK, Kiem PV, Minh CV, Yen PH, Cuong NX, Huong HT. A new flavan glucoside from Glochidion eriocarpum. J. Chem. 2010;48:125-31

Van Wagenen BC, Larsen R, Cardellina JH. II; Randazzo, D.; Lidert, ZC; Swithenbank, C. J. Org. Chem. 1993;58:335-7

Venkateswaran PS, Millman I, Blumberg BS. Effects of an extract from Phyllanthus niruri on hepatitis B and woodchuck hepatitis viruses: in vitro and in vivo studies. Proceedings of the National Academy of Sciences. 1987;84(1):274-8

Yang CM, Cheng HY, Lin TC, Chiang LC, Lin CC. The in vitro activity of geraniin and 1, 3, 4, 6-tetra-O-galloyl-β-d-glucose isolated from Phyllanthus urinaria against herpes simplex virus type 1 and type 2 infection. Journal of ethnopharmacology. 2007;110(3):555-8