Journal of Scientific and Innovative Research 2014; 3(3): 357-362
Available online at: www.jsirjournal.com

Review Article

ISSN 2320-4818
JSIR 2014; 3(3): 357-362

Received: 09-05-2014
Accepted: 10-06-2014

Palmer Sivoko Imbenzi
Chemistry Department, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, P.R. China

Eric Kibagendi. Osoro
Chemistry Department, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, P.R. China

Naji Said Aboud
Chemistry Department, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, P.R. China

Japheth Omollo Ombito
Chemistry Department, Egerton University, P.O. Box 536 Egerton, Kenya

Peter Kiplagat Cheplogoi
Chemistry Department, Egerton University, P.O. Box 536 Egerton, Kenya

Correspondence:
Palmer Sivoko Imbenzi
Chemistry Department, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, P.R. China
Tel: +254733177051
E-mail:
palmersivoko@yahoo.co.uk

A review on chemistry of some species of genus *Vepris* (Rutaceae family)

Palmer Sivoko Imbenzi, Eric Kibagendi Osoro, Naji Said Aboud, Japheth Omollo Ombito, Peter Kiplagat Cheplogoi*

Abstract

This review presents the current known phytochemical constituents of the genus *Vepris*. The genus is a rich source of alkaloids and limonoids most of which possess the 3, 4-methylenedioxy moieties. They are frequently used as antimalarial in African traditional medicine. The genus *Vepris* produces a number of metabolites in high quantities whose biological activities including antiplasmodial and antioxidant activities exhibited are discussed. The ethnopharmacology and toxicity of *Vepris* are also considered.

Keywords: *Vepris*, Alkaloids, Limonoids, Antiplasmodial, Antioxidation.

Introduction

The genus *Vepris* (Rutaceae family) ex A. Juss. comprises some 80 species of shrubs and trees, occurring primarily in tropical Africa, Zanzibar, Madagascar, the Mascarene Islands, and to a lesser extent in tropical Arabia and southwest India.[1] Ethnomedicinally, species of the genus Vepris are employed in the treatment of a diverse range of ailments, including pneumonia, lung diseases and kidney disorders[2], eye troubles, cardiac pains, coughs, colds and influenza[3, 4], headache[5], menorrhagia and infertility[6], as an aphrodisiac[7], diuretic and antipyretic[8], astringent and fortifier[9], tonic[10] for angina and rheumatism[4], and both orally and externally as a treatment for malaria[10]. Limonoids are the main constituents of the Rutaceae and are known to have a wide range of biological activities. The biological activities of limonoids have attracted widespread scientific interest; they are reported to exhibit anti fungal[11], antibacterial[12], antimalarial[13], antifeedant[14], antiprotozoan[15], antiviral[16] and anti-inflammatory activities[17], and recently, the antioxidant capacity of citrus limonoids and limonoid-containing extracts have been evaluated using the racimat experiment, superoxide radical quenching and the Diphenylpropylhydrazyl radical scavenging assays.[18] Limonoids have also been known to inhibit the development of cancer in laboratory animals and in human breast cancer cells.[19]

Fifteen Vepris species have previously been investigated: *V. ampody*[20], *V. binoculars*[21-24], *V. dainellii*[25], *V. elliotii*[7], *V. fitoravina*[26], *V. glomerata*[25], *V. heterophylla*[8, 27-29], *V. leandriana*[30], *V. louisii*[31-36], *V. macrophylla*[26], *V. madagascarica*[37], *V. pilosa*[38], *V. punctata*[1], *V. sclerophylla*[39], *V. stolzii*[40]. Although furoquinoline alkaloids are the most common isolates, acridine and quinol-2-one alkaloids, limonoids and triterpenoids have also been found.[41]

Medicinal importance and bioactivity of some of the isolated metabolites from *Vepris* species

a.) *Vepris uguenensis*

The plant *Vepris uguenensis* known as 'Chemchir' among the Pokot tribe of Kenya has been used traditionally for malaria treatment.[42] From the roots of *V. uguenensis*, a novel antimalarial active limonoid (methyl uguenenoate) **(1)**, an azole (uguenenazole) **(2)** and an imide (uguenenonamide) **(3)** were isolated. Methyl uguenenoate displayed mild antimalarial activity while the azole and the imide were found to be completely inactive. Known furoquinolines alkaloids: flindersiamine **(4)** and maculosidine **(5)** were also isolated. Although compound 4 lacked anti-malarial efficacy against all tested strains, maculosidine **(5)** exhibited moderate anti-malarial activity against two strains of *P. falciparum*, with IC_{50} values of 29.2 and 40.4 μg mL-1 against the chloroquine-susceptible 3D7 and the chloroquine-resistant FCM29 strains respectively (Fig. 1).

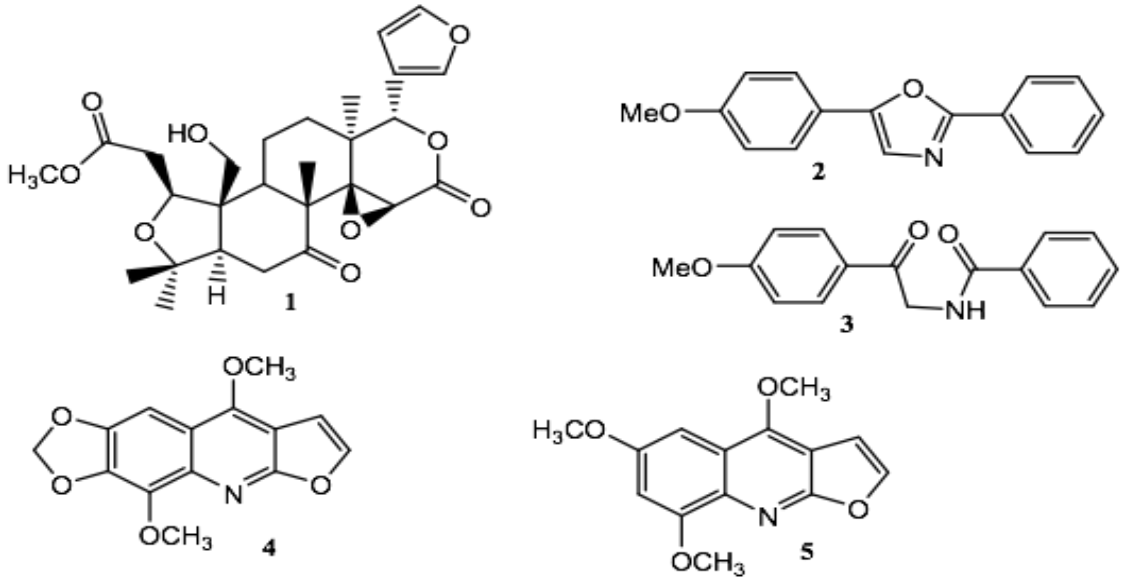

Figure 1: Isolated compounds from *Vepris uguenensis*

b.) *Vepris punctata*

Furoquinoline, Flindersiamine **(4)** isolated from *V. punctata*[43] has shown anti-bacterial activity against Staphylococcus aureas and Streptococcus faecials[44]. Some triterpenoids such as Lupeol (**6)** have been isolated from the same plant[45] and have exhibited cytotoxic activity against Hep-G2, A-431 and H-4IIE tumour cell line. The mechanism of cytotoxic activity of lupeol has been determined to be through the inhibition of topoisomerase II.[46] The root bark of *V. punctata* produced Taraxerol **(7)**[47] which has been reported as a potential cancer chemopreventive constituent[48]. Glechomanolide **(8)** isolated from the same species has shown cytotoxicity (Fig. 2).[47]

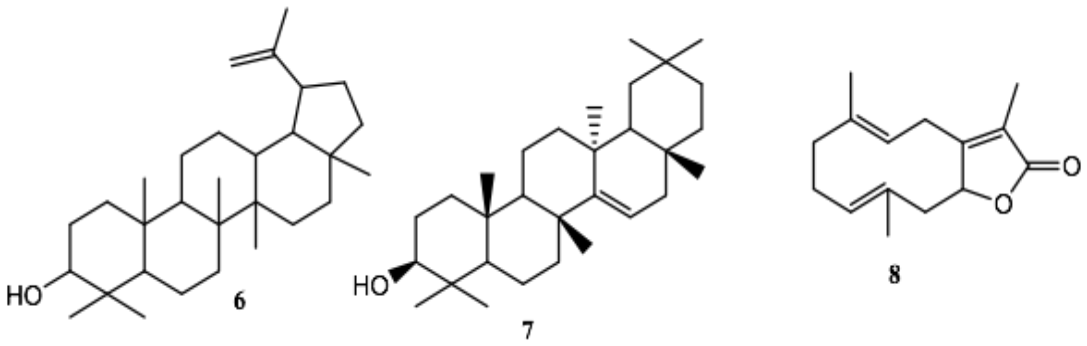

Figure 2: Isolated compounds from *Vepris punctata*

c.) *Vepris glomerata*

The dichloromethane extract of the aerial part of the plant *Vepris glomerata* yielded a new flavonoid, veprisinol **(9)**, together with four known furoquinoline alkaloids: isohaplopine-3,3'-dimethylallyl ether **(10)**, tecleoxine **(11)**, nkolbisine **(12)** and skimmianine **(13)**.[49] Compounds 9 and 10 had strong antioxidant potential, similar to and in some instances better than ascorbic acid and can therefore be used as beneficial additives to antioxidant supplements (Fig. 3).

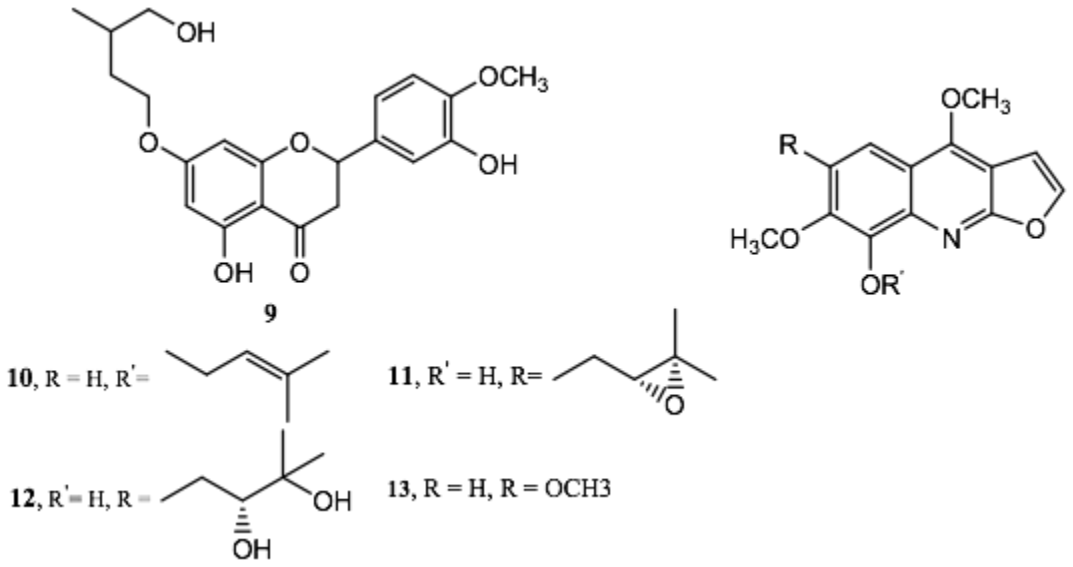

Figure 3: Isolated compounds from *Vepris glomerata*

d.) *Vepris louisii*

The dihydrofuroquinoline alkaloid Veprisinium chloride **(14)** isolated from *V. louisii* exhibited antibacterial activity.[33] Veprisine **(15)** isolated from *V. louisii*[34] has also shown cytotoxic activity.[50] From the bark of *V. louisii*, N-methylpreskiammine **(16)** and veprisilone **(17)** were also isolated (Fig. 4).[31]

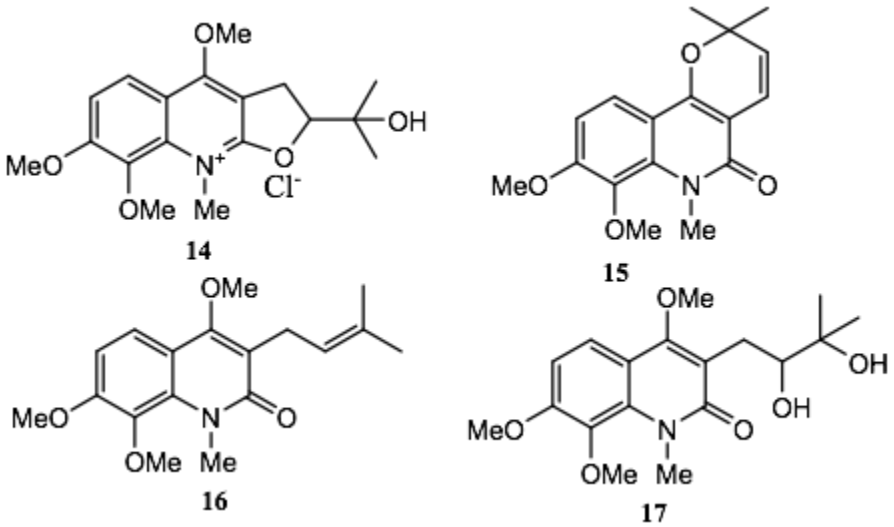

Figure 4: Isolated compounds from *Vepris louisii*

e.) *Vepris ampody*

Vepris ampody H. Perr. is a 15 to 20 m tall tree, with perennial foliage, often reduced to a shrub in the undergrowth of the big forest. It's a special species of Madagascar, very common in the eastern forest from sea level to 600 m of altitude. Known in malagasy by the names of Ampody (Bezanozano dialect) or Malaimbovony

(Betsimisaraka dialect), it provides good construction wood. From the leaves and branches of *V. ampody*, four known alkaloids, viz. N,N-dimethyltryptamine **(18)**, kokusaginine **(19)**, 2,4-dimethoxy-10-methyl-acridan-9-one **(20)** and phenylacetamide **(21)** were isolated (Fig. 5).[20]

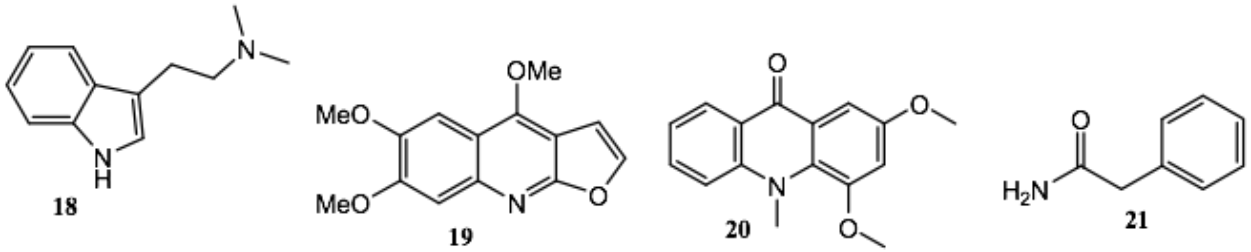

Figure 5: Isolated compounds from *Vepris ampody*

f.) *Vepris fitoravina*

Vepris fitoravina H. Perr endemic species growing in Malagasy, is used in folk medicine as "euphoristic" drugs.[51] From the leaves of *Vepris fitoravina*, four acridone alkaloids arborinine **(22)**, evoxanthine **(23)**, 1 ,3-dimethoxy-10-methylacridan-9-one **(24)** and 1-hydroxy-2,3,4-trimethoxyacridan-9-one **(25)** were isolated.[26] Although Koffi and co-workers did not test the activity of these acridones against any microorganisms, some of these acridones such as arborinine has shown mild but significant in vitro antibacterial activity and exhibited moderate cytotoxicity (Fig. 6).[52]

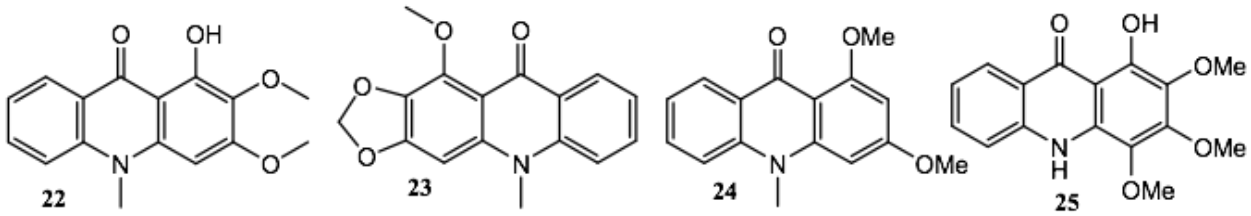

Figure 6: Isolated compounds from *Vepris fitoravina*

Conclusion

Genus *Vepris* is a rich source of phenolic compounds, mainly alkaloids, limonoids, flavonoids and their derivatives. Besides, these compounds have been linked to most of the pharmacological activities including significant antioxidant activities. As a result, Vepris plants should be explored further as an alternative source of medicine.

Acknowledgement

The authors thank the Ministry of Education in China through the Chinese Scholarship Council for the grants, the Departments of Chemistry of Tianjin University of Traditional Chinese Medicine and Egerton University, Kenya for facilitating a conducive research environment.

References

1. Chaturvedula, V.S.P., Schilling, J.K., Miller, J.S., Andriantsiferana, R., Rasamison, V.E., Kingston D.G.I.. New cytotoxic alkaloids from the wood of *Vepris punctata* from the Madagascan rainforest. J. Nat. Prod. 2003; 66: 532-534.

2. Hedberg, I., Hedberg O., Madati P.J., Msigeni, K.E., Mshiu E.N., Samuelsson G.. Inventory of plants used in traditional medicine in Tanzania. Part III. Plants of the families Papilionaceae-Vitaceae. Journal of Ethnopharmacology 1983; 9: 237-260.

3. Chhabra, S.C., Mahunnah, R.L., Mshiu, E.N.. Plants used in traditional medicine in eastern Tanzania. *V. Angiosperms* (Passifloraceae to Sapindaceae). Journal of Ethnopharmacology 1991; 33: 143-57.

4. Gurib-Fakim, A., Sewraj, M., Gueho, J., Dulloo, E.. Medical ethnobotany of some weeds of Mauritius and Rodrigues. Journal of Ethnopharmacology 1993; 39: 175-85.

5. Arnold, H.J., Gulumian, M.. Pharmacopoeia of traditional medicine in Venda. Journal of Ethnopharmacology 1984; 12: 35-74.

6. Steenkamp, V.. Traditional herbal remedies used by South African women for gynaecological complaints. Journal of Ethnopharmacology 2003; 86: 97-108.

7. Poitou, F., Masotti, V., Viano, J., Gaydou, E.M., Andriamahavo, N.R., Mamitiana, A., Rabemanantsoa, A., Razanamahefa, B.V., Andriantsiferana, M.. Chemical Composition of *Vepris elliotii* essential oil. Journal of Essential Oil Research 1995; 7: 447-449.

8. Gomes, E.T., Travert, S., Gleye, J., Moulis, C., Fouraste, I., Stanislas, E.. Furoquinoline alkaloids from *Vepris heterophylla*. Planta Medica 1994; 60: 388.

9. Vera, R., Smadja, J., Conan, J.Y.. Preliminary screening of alkaloid-containing plants of Reunion. Plantes Medicinales et Phytotherapie 1990; 24: 50-65.

10. Gessler, M.C., Nkunya, M.H., Mwasumbi, L.B., Heinrich, M., Tanner, M.. Screening Tanzanian medicinal plants for antimalarial activity. Acta tropica 1994; 65-77.

11. Abdelgaleil, S.A.M., Hashinaga, F., Nakatani, M.. Antifungal activity of limonoids from *Khaya ivorensis*. Pest Manage. Sci. 2005; 61: 186–190.

12. Rahman, A.K.M.S., Chowdhury, A.K.A., Ali, H.A., Raihan, S.Z., Ali, M.S., Nahar, L., Sarker, S.D.. Antibacterial activity of two limonoids from *Swietenia mahagoni* against multiple-drug (MDR) bacterial strains. J. Nat. Med. 2009; 63: 41–45.

13. Bickii, J., Tchouya, G.R.F., Tchouankeu, J.C., Tsamo, E.. The antiplasmodial agents of the stem bark of *Entandrophragma angolense* (Meliaceae). Afr. J. Tradit. Complement. Altern. Med. 2007; 4: 135–139.

14. Abdelgaleil, S.A.M., Okamura, H., Iwagawa, T., Doe, M., Nakatani, M.. Novel rings B, D-seco limonoids from the stem bark of *Khaya senegalensis*. Heterocycles 2000; 53: 2233–2240.

15. Khalid, S.A., Friedrichsen, G.M., Kharazmi, A., Theander, T.G., Olsen, C.E., Christensen, S.B.. Limonoids from *Khaya senegalensis*. Phytochemistry 1998; 49: 1769–1772.

16. Nakatani, M., Abdelgaleil, S.A.M., Kurawaki, J., Okamura, H., Iwagawa, T., Doe, M.. Antifeedant rings B and D opened limonoids from *Khaya senegalensis*. J. Nat. Prod. 2001; 64: 1261–1265.

17. Akihisa, T., Noto, T., Takahashi, A., Fujita, Y., Banno, N., Tokuda, H., Koike, K., Suzuki, T., Yasukawa, K., Kimura, Y.. Melanogenesis inhibitory, anti-inflammatory, and chemopreventive effects of limonoids from the seeds of *Azadirachta indicia* A. Juss (Neem). J. Oleo Sci. 2009; 58: 581–594.

18. Breksa, A.P., Manners, G.D.. Evaluation of the Antioxidant capacity of limonin, nomilin, and limonin glucoside. J. Agric. Food Chem. 2006; 54: 3827–3831.

19. Zhang, H., Wang, X., Chen, F., Androulakis, X.M., Wargovich, M.. Anti-cancer activity of *Khaya senegalensis*. Phytother. Res. 2007; 21: 731–734.

20. Kan-Fan, C., Das, B.C., Boiteau, P., Potier, P.. Alcaloïdes de *Vepris ampody* (Rutacées). Phytochemistry 1970; 9: 1283-1291.

21. Govindachari, T.R., Sundararajan, V.N.. Alkaloids of *Vepris bilocularis*. Journal of Scientific and Industrial Research 1961; 20B: 298-299.

22. Govindachari, T.R., Joshi, B.S., Sundararajan, V.N.. Structure of veprisone, a constituent of *Vepris bilocularis*. Tetrahedron 1964; 20: 2985-2990.

23. Ganguly, A.K., Govindachari, T.R., Manmade, A., Mohamed, P.A.. Alkaloids of *Vepris bilocularis*. Indian Journal of Chemistry 1966; 4: 334-335.

24. Brader, G., Bacher, M., Greger, H., Hofer, O.. Pyranoquinolones and acridones from *Vepris bilocularis*. Phytochemistry 1996; 42: 881-884.

25. Dagne, E., Yenesew, A., Waterman, P.G., Gray, A.I.. The chemical systematics of the Rutaceae, subfamily Toddalioideae, in Africa. Biochemical Systematics and Ecology 1988; 16: 179-188.

26. Koffi, Y., Gleye, J., Moulis, C., Stanislas, E.. Acridones from Vepris fitoravina and *Vepris macrophylla*. Planta Medica 1987; 53: 570.

27. Gomes, E., Dellamonica, G., Gleye, J., Moulis, Cl., Chopin, M.J., Stanislas, E.. Phenolic compounds from *Vepris heterophylla*. Phytochemistry 1983; 22: 2628-2629.

28. Moulis, C., Fouraste, I., Keita, A., Bessiere, J. M.. Composition of the leaf essential oil from *Vepris heterophylla* R.Let. Flavour and Fragrance Journal 1994; 9: 35-37.

29. Sidibe, L., Chalchat, J-C., Garry, R-P., Harama, M.. Aromatic plants of Mali. VI. Chemical composition of essential oil of *Vepris heterophylla* 2001. (Engl.).

30. Rakotondraibe, L.H.R., Rakotovao, M., Ramanandraibe, V., Ravaonindrina, N., Frappier, F., Brouard, J-P.. Composition and antimicrobial activity of leaf oils of *Vepris leandriana* H. Perr. Journal of Essential Oil Research 2001; 13: 467-469.

31. Ayafor, J.F., Sondengam, B.L., Ngadjui, B.T.. Veprisine and N-methylpreskimmianine: Novel 2-quinolones from *Vepris louisii.* Tetrahedron Letters 1980; 21: 3293-3294.

32. Ayafor, J.F., Sondengam, B.L., Ngadjui, B.T..The structure of veprisinium salt. Tetrahedron Letters 1981; 22: 2685-2688.

33. Ayafor, J.F., Sondengam, B.L., Ngadjui, B.T.. Veprisinium salt, a novel antibacterial quaternary alkaloid from *Vepris louisii*. Planta Medica 1982a; 44: 139-142.

34. Ayafor, J.F., Sondengam, B.L., Ngadjui, B.T.. Veprisilone, a prenylated 2-quinolone, and limonin from *Vepris louisii*. Phytochemistry 1982b; 21: 955-956.

35. Ayafor, J.F., Sondengam, B.L., Ngadjui, B.T.. Quinoline and indolopyridoquinazoline alkaloids from *Vepris louisii*. Phytochemistry 1982c; 21: 2733-2736.

36. Ngadjui, T.B., Ayafor, J.F., Sondengam, B.L., Connolly, J.D., ; Rycroft, D.S., Khalid, S.A., Waterman, P.G., Brown, N.M.D., Grundon, M.F., Ramachandran, V.N.. The structures of vepridimerines A-D, four new dimeric prenylated quinolone alkaloids from *Vepris louisii* and *Oricia renieri* (Rutaceae). Tetrahedron Letters 1982; 23: 2041-2044.

37. Billet, D., Favre-Bonvin, J.. Constituants de l'huile essentielle de *Vepris madagascarica*. Phytochemistry 1973; 12: 1194.

38. Haensel, R., Cybulski, E.M.. Alkaloids from the root bark of Vepris pilosa. Archiv der Pharmazie (Weinheim, Germany) 1978; 311: 135-138.

39. Rasoanaivo, P., Federici, E., Palazzino, G., Galeffi, C.. Acridones of *Vepris sclerophylla*: their 13C NMR data. Fitoterapia 1999; 70: 625-627.

40. Khalid, S.A., Waterman, P.G.. Chemosystematics in the Rutaceae. 15. Furoquinoline and pyrano-2-quinolone alkaloids of *Vepris stolzii*. Journal of Natural Products 1982; 45: 343-346.

41. Dictionary of Natural Products on CD-ROM. Chapman Hall/CRC Press/Hampden Data Services, Ltd. 2007; version 16.1.

42. Cheplogoi, P. K., Mulholland; D.A., Coombes, P.H. and Randrianarivelojosia, M.. An azole, an amide and limonoids from *Vepris uguenensis* (Rutaceae).Phytochemistry 2008; 69: 1384 –1388.

43. Prakash V., Pain D.J., Cunningham A.A., Donald P.F., Prakash N., Verma A., Gargi R., Sivakumar S., Rahmani A.R. Catastrophic collapse of Indian white-backed *Gyps bengalensis* and long-billed *Gyps indicus* vulture populations. Biological Conservation 2003; 109(3): 381-390.

44. Aguilar-Guadarrama, Rios M.Y. and A. Berenice; 1H and 13C assignments of two new triterpenes from *Cladocolea grahami*. Magnetic Resonance in Chemistry 2004; 42(12): 1066-1068.

45. Chaturvedula VSP, Schilling JK, Miller JS, Andriantsiferana R, Rasamison VE, Kingston DGI. New cytotoxic terpenoids from the wood of *Vepris punctata* from the Madagascar rainforest. Journal of Natural Products. 2004a; 67: 895-898.

46. Moriarity, D.M., Huang, J., Yancey, C.A., Setzer, W.N., Lawton, R.O., Bates, R.B. and Caldera, S.. Lupeol is the cytotoxic principle in the leaf extract of *Dendropanax cf. querceti.* Planta Medica 1998; 64: 370-372.

47. Chaturvedula VSP, Zhou B, Gao Z, Thomas SJ, Hecht SM, Kingston DGI. New lupane triterpenoids from Solidago condenses that inhibit the lyase activity of DNA polymerase Beta. Bioorganic Medicinal Chemistry 2004b; 12: 6271-6275.

48. Jang, D.S., Cuendet, M., Pawlus, A.D., Kardono, L.B., Kawanishi, K., Farnsworth, N.R., Fong, H.H., Pezzuto, J.M. and Kinghorn, A.D.. Potential cancer chemopreventive constituents of the leaves of *Macaranga triloba*. Phytochemistry 2004; 65: 345-350.

49. Kiplimo. J. J., Shahidul I. Md., Neil A. K.. Ring A-seco limonoids and flavonoids from the Kenyan *Vepris uguensis* Engl. and their antioxidant activity. Phytochemistry 2012; 83: 136-143.

50. Setzer, W.N., Volger, B., Bates, R.B., Schmidt, J.M., Dicus, C.W., Nakkiew, P. and Haber, W.A.. HPLC-NMR/HPLC-MS analysis of the bark of *Stauranthus perforatus*. Phytochemistry 2003; 14: 54-59.

51. Boiteau, P.. Précis de MatiCreMCdicale Malgache. Librairie deMadagascar. 1979; (ed. Antanananvo), 21.

52. Sohrab, M.H., Chowdhury, R., Rahman, K.M., Hasan, C.M. and Rashid, M.A.. Antibacterial activity and cytotoxicity of extractive from *Ravenia spectabilis*. Fitoterapia 2004; 75: 510-513.