RESEARCH ARTICLE

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An Antioxidant Quinoline Derivative Isolated from Pauridiantha Paucinervis Var. Lyalli (Rubiaceae)

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ABSTRACT

Pauridiantha paucinervis var. Lyalli (Rubiaceae)[1][2] is a plant abounding in alkaloid compounds[3] of which the quinoline derivatives are the majority. An alkaloid quinoline has been isolated for the first time of this plant. The chemical formula of this compound is $C_{26}H_{30}N_2O_9$ while its mass is M = 514. This plant can be found and bought everywhere at the markets and at the herbalists on the island. It is a widely known plant of the Malagasy traditional medicine. The structure has been clarified by analyses of its NMR 1D and 2D as well as ESI-MS (coupled with HPLC) spectral data. The test with the DDPH reagent on a thin layer of silica gel chromatogram revealed that the isolated substance has antioxidant activity [4]-[8].

Keywords: Antioxidant, ESI-MS, NMR, Pauridiantha, Quinoline, Rubiaceae.

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I. Introduction

Madagascar is fully endowed with in medicinal plants of which more than 30% are endemic. They have been usually prescribed by the traditional medicine for a long time. Unfortunately, every year, this immense flora is devastated by the practice of slash and burn, called “tavy” in Malagasy, while only a small amount of these treasures has been studied scientifically. One distinguishes among these plants, Pauridiantha paucivernis var. Lyalli, belonging to the family Rubiaceae. It is commonly used by the traditional medicine and sold by the herbalists of several markets in Madagascar. Its leaves are used to cure various illnesses such as the fever, the spiders’ and scorpions’ bites, the stomach and joint pains.

II. Materials and Methods

A. Extraction and Purification

The studied plant is bought at the market of Antananarivo city. A voucher is identified and deposited at the Botanical and Zoological Park of Tsimbazaza Antananarivo Madagascar.

First of all, the dry plant powder (3.124 Kg) is washed with a Soxhlet device with hexane for 2 X 30 minutes so as to obtain the hexane excerpt (Ehex(hexane extract) = 120.7 g). The remaining washed powder is extracted then by reflux distillation with chloroform for 2 × 30 minutes with a view to having the chloroform excerpt (EChl(chloroform extract) = 201.5 g).

The chemical components of these two excerpts are observed on thin layer silica gel chromatography of Merck 60 F254, developed respectively in hexane/ ethyl acetate mixture 8/2 (v/v) for the first excerpt and in chloroform/methanol 9/2 (v/v) for the second.

On silica gel chromatogram revealed with Dragendorff reagent, the excerpt of chloroform (EChl) shows an alkaloid the quantity of which is most important than the other. This compound is then targeted to be purified. This excerpt is chromatographed on silica gel column (50 × 3.5 centimeters) with chloroform/methanol 8/2 (v/v) mixture as eluent. All collected fractions containing the product target are concentrated and then chromatographed again on silica gel column (15 × 2 centimeters) eluted with Chloroform/methanol 9/1 (v/v) in order to get the pure targeted product. The progress of the column chromatography is followed on silica gel thin layer chromatography that is visualized under UV lamp 254/366 nm and revealed by pulverization with Dragendorff reagent later on. The resulting pure product (14.3 mg) has an amorphous white powder aspect. The determination of its structure has been carried out through analysis of its 1D and 2D NMR spectra recorded on a Bruker A400 device that uses TMS as internal reference and CD3OD as solvent.

III. Results and Discussion

A. Elucidation of the Structure

The structure determination has been divided in two stages and effectuated by means of NMR HMQC, COSY and HMBC spectral data analysis. The first sub-structure consists to the structure identification of a déhydropyran O-methyl carboxylate derivative and the structure of a quinoline derivative represents the second one.

The sub-structure 1 contains a 17,18-déhydropyran derivative. in fact, the 3JHH NMR COSY correlations between H-13(3.352;33.5) and H-14(2.621;44.2) then H-14(2.621;44.2) with H-15(5.779; 96.1) also the 3JCH NMR HMBC correlations that exist between H-13(3.352;33.5) and [C-15(96.1),C-17(153.2)] and between H-14 and C-18(109.2) affirm the existence of a dehydropyran. Also the abnormally higher values of the chemical shift of C-15(96.1) and C-17(153.2) due to the presence of an oxygen atom O-16, confirm the presence of the dehydropyran. The NMR HMBC correlations between H-13(3.352; 33.5) and [C-15(96.1), C-17(153.2)] then between H-14(2.621;44.2) and C-18(109.2) affirm this hypothesis. Also, one β-D-Glucose is identified by comparison of its 13C and 1H NMR chemical shifts with those of model compounds [9].

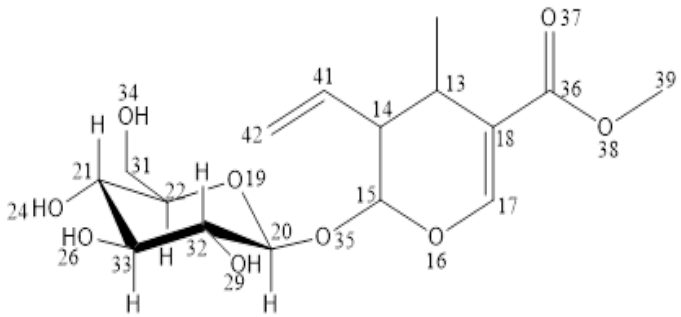

Fig. 1. Sub-structure part-1: 15-O-Glycosyl-14-vinyl-14,15-dihydropyran-18 (O-methyl) carboxylate.

The HMBC correlation that has H-15(5.779;96.1) with C-20(98.8) which is an anomeric carbon of the β-D-Glucose certifies also this assertion. The HMBC correlations between H-13(3.352;33.5) and [C-17(153.2);C-18(109.2)] and the chemical shift value of C-17 and C-18, inform that a double bound is localized between C-18(109.2) and C-17(153.2). Besides, the HMBC correlations that H-13(3.352;33.5) has with C-41(134.0) like H-14(2.621;44.2) with C-42(118.3) enabled to emphasize that the carbon C-14(44.2) of the dehydropyran is linked to a vinyl group constituted by C-41(134.0) and C-42 (118.3). The HMBC correlations of H-13(3.352 ;33.5) and H-17(7.541;153.2) with a carbonyl C-36(168.0), permit to

approve that C-18(109.2) is bounded with an O-methyl carboxylate constituted by a carbonyl C-36 (168.0) and an O-methyl C-39(50.6).

Part 2 of the structure, which is a derivative of the quinoline, is established by the analysis of COSY and HMBC NMR data.

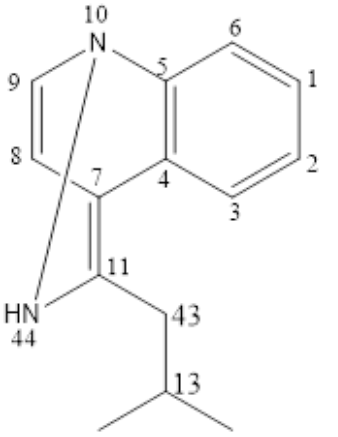

Fig. 2. Sub-structure part-2: 11-isobutyl-1, 7 - (epiminometheno) quinolone.

The unsaturated and unsubstituted carbon positions C-1(128.8), C-2(119.9), C-3(121.7) and C-6(111.8) are typical of quinoline derivatives. They are also confirmed by the correlations COSY NMR that H-1(7.593) has with H-6(7.627;128.8) and H-2(7.301;119.9), then between H-2(7.301) and H-3(8.172;121.7)). A double bound is localized between C-8(113.5) and C-9(135.1) which is supported by the HMBC correlations between H-9(8.250;135.1) and C-7(129.8) and between H-8(8.032;113.5) and [C-4(120.8);C-11(142.8)]. These correlations also demonstrate the presence of a double bound between C-7(129.8) and C-11(142.8). The nitrogen N-10 provokes the increase of the chemical shifts value of the carbons C-5(141.5) and C-9(135.1). In the same way, the nitrogen N-44 amplifies the increase of the chemical shifts value of C-11(142.8) and C-7(129.8). The carbon C-11 (142.8) is bound with a isobutyl group. This bound presence is confirmed by the NMR HMBC correlations between H-13(3.352; 33.5) and C-11(142.8) and the ones between H-14(2.621; 44.2) and C-43(33.7).

The combination of the two sub-structure 1 and 2 allows to have the whole structure of the isolated compound. This structure is illustrated below (Fig. 3).

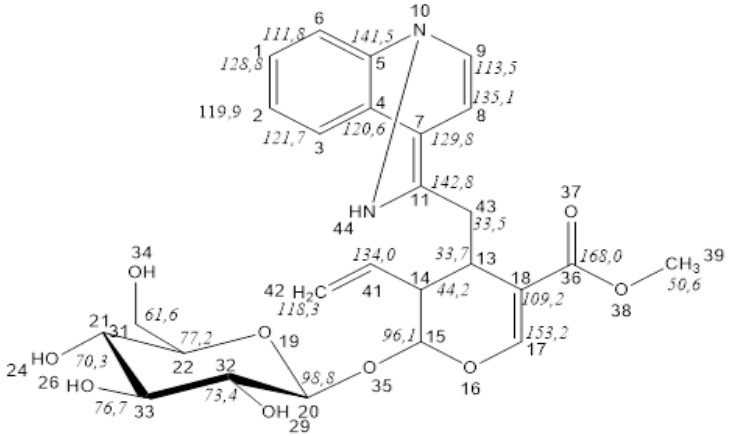

Fig. 3. Structure of the isolated compound.

This structure is also endorsed by the spectral data analysis of ESI-MS coupled with HPLC. According to its chemical formula $C_{26}H_{30}N_2O_9$, the isolated substance would have a molecular mass M = 514. However, the ESI-MS spectrum shows a mass equal to 528. The mass difference ΔM = 14 can be assigned to the presence of an adduct carbene CH_2 that appeared during the registration of the mass spectrum. Indeed, the highest peak of the spectrum (528) corresponds therefore to M + CH_2. Besides, the ESI-MS spectrum presents a peak at 1053. This peak informs that there is formation of a dimer. Considering the mass M + 14 = 528, the dimer mass should be 1056. However, the dimerization reaction required the departure of 4 hydrogen atoms that gave a molecular mass of the dimer D = 1052. The peak at 1053 is assigned therefore $C_{26}H_{30}N_2O$ to the mass of D + H = 1053. This spectral data ESI-MS analysis permitted to confirm the molecular mass M = 514 of the quinoline derivative as well as its chemical formula $C_{26}H_{30}N_2O$.

B. Test of the Antioxidant Activity

The test by pulverization with the 2,2-diphényl 1-picrylhydrazine (DDPH) reagent on a chromatogram of silica gel that gave a pale-yellow coloration, pointed out that the isolated substance is antioxidant.

IV. Conclusion

There is a great advantage to conducting research on plants that have already been used by the traditional medicine for years. Indeed, their use would be forbidden if they are toxic, present signs of intolerance or the secondary effects. The studied plant Pauridiantha paucinervis var. Lyalli is prescribed to cure several illnesses and it is sold at the markets and the herbalists of Madagascar. A quinoline derivate compound has been isolated, for the first time, of the chloroform extract of this plant. The HSQC, COSY and HMBC NMR as well as the ESI-MS spectral data analysis enable to clarify its structure. The amorphous white powder purified product has a mass M = 514 and an activity antioxidant. This later is revealed on silica gel chromatogram through pulverization with the 2,2-diphényl 1-picrylhydrazine (DDPH) reagent.

Appendix

A. NMR C^{13}

δ (C ppm): 128,8 (C-1); 119,9(C-2); 121,7(C-3); 120,6(C-4); 141,5(C-5); 111,8(C-6); 129,8(C-7); 113,5(C-8); 135,1(C-9); 142,8(C-11); 33,5(C-13); 44,2(C-14); 96,1(C-15); 153,2(C-17); 109,2(C-18); 98,8(C-20); 70,3 (C-21); 77,2(C-22); 61,6(C-31); 73,4(C-32); 76,7(C-33); 168,0(C-36); 50,6(C-39); 134,0(C-41); 118,3(C-42); 33,7(C-43)

B. NMR H^{1}

δ (H ppm): 7,593 (H-1, t); 7,301(H-2, t); 8,172(H-3); 7,627(H-6, D); 8,032(H-8, D); 8,250(H-9, d); 3,352(H-13, q); 2,621(H-14, q); 5,779(H-15, d); 7,541(H-17, s); 4,780(H-20, d); 3,33(H-21, t); 3,39(H-22, Td); 3,933-3,694(H-31, d, q); 3,26(H-32, T); 3,427(H-33, T); 3,33(H-39, s); 5,886(H-41, t); 5,043(H-42,dd); 3,516(H-43, d)

C. ESI-MS Spectrum (Fig. 3)

M(z): 101
101,0446
223,0668
302,9943
527,1284
528,1450
703,1212
733,1421
734,1608
735,1603
751,1647

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