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Prenylated 2-arylbenzofuran derivatives with potent antioxidant properties from *Chlorophora regia* (Moraceae)

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ABSTRACT

Extracts of *Chlorophora regia* are frequently used in Ghana in traditional medicine. There is, however, no reported data on the chemical composition of the plant. Comprehensive phytochemical investigation of the stem bark of *C. regia* resulted in the isolation of three new prenylated 2-arylbenzofuran derivatives, regiafuran A–C (**1–3**), and one new prenylated flavonol (**4**), together with fifteen known compounds (**5–19**). Their structures were elucidated by combined spectroscopic analysis of their NMR and HRESI-MS^n data. Compounds **1, 2, 5, 9** and **15** exhibited remarkable free radical scavenging properties with IC_{50} values of 1.9 μg/ml, 2.4 μg/ml, 2.2 μg/ml, 2.1 μg/ml and 1.8 μg/ml, respectively, compared to the standard trolox (IC_{50} 1.1 μg/ml). The isolated compounds did not, however, show any anti-inflammatory potential when tested using a PGE_2 (prostaglandin E_2) competitive enzyme immunoassay.

1. Introduction

Chlorophora regia is a large dioecious tree of about 35–45 m belonging to the family Moraceae. The tree is widely distributed across tropical West Africa and indigenous to the forest zone of Senegal, Gambia and Ghana. The bole is usually straight and cylindrical, often branchless for more than 20 m, up to 2 m in diameter, without buttresses but spurs may become very large and extend into long surface roots [1]. It is locally known as *Odum-nua* (Akan dialect) in Ghana. *C. regia* is a highly important commercial timber in Africa and the timber obtained from this plant is used in the furniture industry [2]. It is also used indigenously for producing charcoal and as fire wood [1]. Traditionally, extracts of the stem bark is used for the treatment of burns and wounds, snake bite, wasp bite and syphilis. Extract of the root bark has been reported to be active against *Staphylococcus aureus* [3].

Although some species in the genus have been investigated, there is no report in literature, to the best of our knowledge, of the chemical composition of this medicinal plant. Many genera in the Moraceae family are rich sources of phenolic compounds [4,5] and the *Chlorophora* genus is no exception. In the present report, an investigation to establish a comprehensive chemical composition and to contribute to the chemotaxonomy of the Ghanaian medicinal plant *C. regia*, resulted in the isolation and characterization of three new 2-arylbenzofuran derivatives, regiafuran A–C (**1–3**) and one new prenylated flavonol, 6–prenylated–3,5,7,4′–tetrahydroxy–2′–methoxyflavonol (**4**) with potent anti-oxidant properties, together with fifteen known bioactive compounds (**5–19**). The structures of the new compounds were established by extensive analysis of their 1D and 2D NMR and HRESI–MS^n spectroscopic data. A tentative biosynthetic pathway of compound **4** was proposed based on the biosynthesis of flavonols [6,7].

2. Results and discussion

A comprehensive phytochemical investigation of the stem bark of *C. regia* led to the identification of three new 2-arylbenzofuran derivatives, regiafuran A–C (**1–3**) and one new prenylated flavonol, 6–prenylated–3,5,7,4′–tetrahydroxy–2′–methoxyflavonol (**4**), together with fifteen known bioactive compounds (**5–19**); mulberrofuran Y (**5**) [8], moracin N (**6**) [9], moracin O (**7**) [10], sanggenon C (**8**) [11], kuwanol E (**9**) [12], chalcomoracin (**10**) [13], chlorophorin (**11**) [14], isochlorophorin (**12**) [6], gancaonin P (**13**) [15], 3,5,7,4′–tetrahydroxy–2′–methoxyflavonol (**14**) [16], 5,7,4′–trihydroxy–2′–methoxyflavanone (**15**) [17], 5,7,3′,5′–tetrahydroxyflavanone (**16**) [18], quercetin (**17**) [19], naringenin (**18**) [20], kaempferol (**19**) [21] (Fig. 1). To the best of our knowledge, this is the first report of compounds **12–16** in the genus *Chlorophora*. Furthermore, compound **14** is a rare flavonoid first isolated from *Anaxagorea luzonensis* A. Gray [16] and was incorrectly named as 3,5,7,4′–tetrahydroxy–2′–

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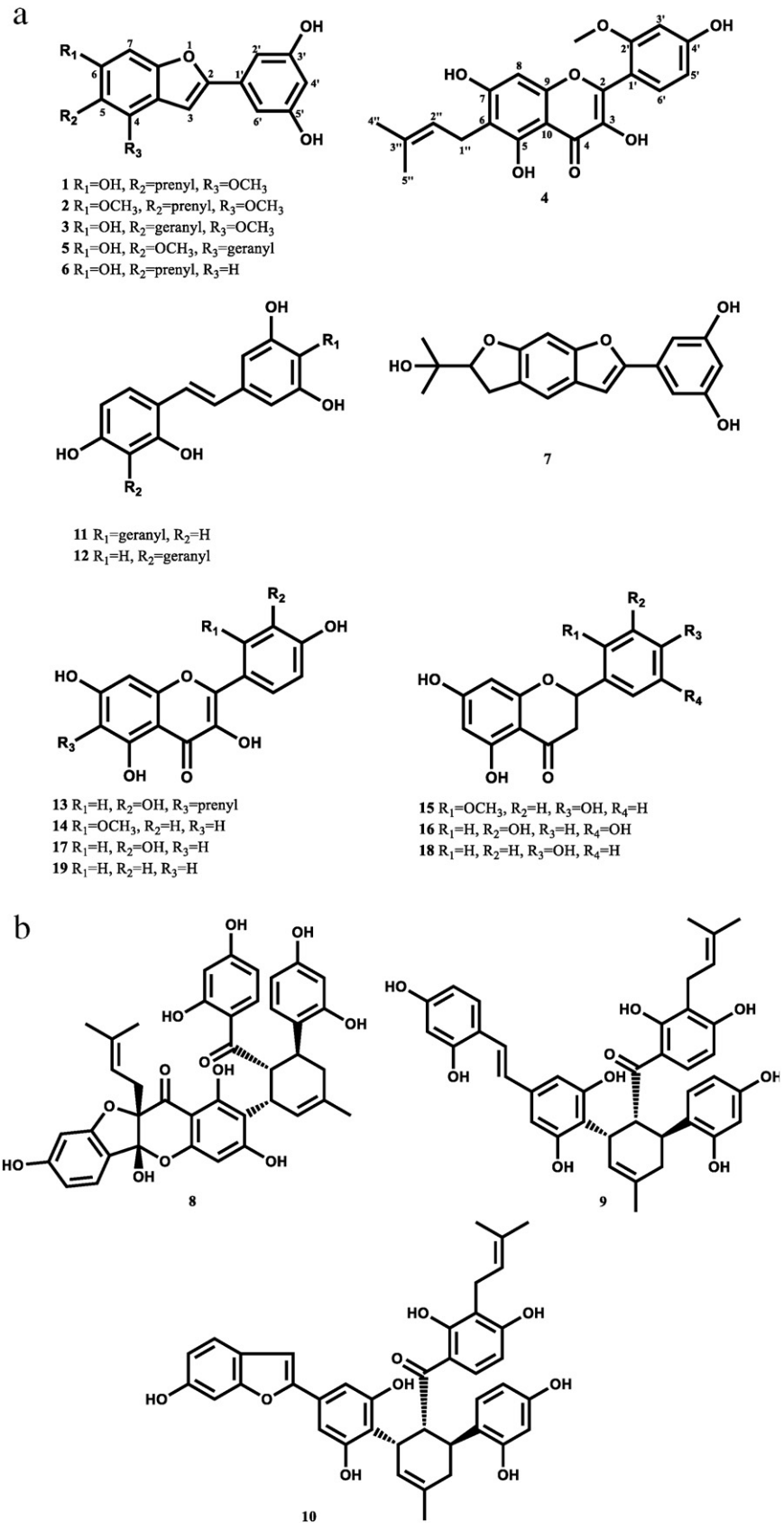

Fig. 1. a: Chemical structures of compounds **1**–**7** and **11**–**19** isolated from *C. regia*. b: Chemical structures of compounds **8**–**10** isolated from *C. regia*.

methoxyflavone. The chemical structure of **14** has a flavonol nucleus and not a flavone nucleus [22–24]. Herein we provide the correct name of **14** as 3,5,7,4′–tetrahydroxy–2′–methoxyflavonol.

Compound **1** was obtained as yellow amorphous solid and the molecular formula was assigned as $C_{20}H_{21}O_5$ based on the ion *m/z* 341.1386 $[M + H]^+$ (calcd. for 341.1384) in the HRESI–MS spectrum.