SHORT REPORT

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Cytotoxic Sesquiterpenoids and Diarylheptanoids from the Rhizomes of *Curcuma elata* Roxb.

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Abstract: The present study was aimed to investigate the chemical constituents of *Curcuma elata* Roxb. (Zingiberaceae) rhizomes originating in Thailand. Ten sesquiterpenes, germacrone (**1**), curzerenone (**2**), isofuranodienone (**3**), furanodienone (**4**), curdione (**5**), neocurdione (**6**), zederone (**7**), curcumenone (**8**), 13-hydroxygermacrone (**9**) and zedoarondiol (**10**), and four diarylheptanoids, 3-hydroxy-5-platyphyllone (**11**), (3*S*)-1,7-*bis*(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol (**12**), centrolobol (**13**) and (3*S*)-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol (**14**) were isolated for the first time from the rhizomes of this plant. The structures of the isolated compounds were identified by comparison of the spectroscopic and physical data with those of the reported values and the stereochemistry at the asymmetric carbon was determined by the modified Mosher's method and, in some cases, was confirmed by comparison of optical rotation data with literature. Compounds **12** and **13** exhibited strong cytotoxic activity against KB cell line, whereas compounds **4**, **9** and **12-14** showed strong cytoxicity against NCI-H187 cell line.

Keywords: *Curcuma elata*; Zingiberaceae; sesquiterpenoids; diarylheptanoids; cytotoxicity.

1. Plant Source

Curcuma is a well known genus of Zingiberaceae family. They are perennials and widely distributed in tropics and subtropics including Thailand. *Curcuma elata* Roxb. is commonly known as "Wan-chak-motluk-tua-phu" in Thai [1]. The rhizomes of this plant species were collected from Sawangdaendin district, Sakon Nakhon province, Thailand in June 2007. The plant was identified by

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Puangpaka Soontornchainaksaeng and Thaya Jenjittikul, Department of Plant Science, Faculty of Science, Mahidol University, Bangkok, Thailand [2]. The voucher specimen (SCMU, No. 305) is deposited at the Department of Plant Science, the Faculty of Science, Mahidol University.

2. Previous Studies

Approximately 20 *Curcuma* species have been studied phytochemically and three major classes are identified, diarylalkanoids, arylpropene derivatives of cinnamic acid type and terpenoids. About 140 different sesquiterpenoids have been isolated from the genus *Curcuma*, and they can be classified into ten distinctly different structural types. However, most of these compounds fall into one of the three major categories, bisabolane, germacrane or guaiane types [3]. The investigations on *Curcuma* which led to the isolation of monoterpenoids [4], sesquiterpenoids [5-8], diterpenoids [9,10], and diarylheptanoids [11-13] have been reported. To our knowledge, there has been no report on phytochemical study and biological activity of *C. elata*. We wish to report on the isolation and structural identification of the sesquiterpenoids **1**-**10** and the diarylheptanoids **11**-**14**.

3. Present Study

The air-dried rhizomes of *C. elata* (8.5 kg) were milled and macerated successively with *n*-hexane and EtOH. The hexane and EtOH solutions were filtered and concentrated to dryness under reduced pressure at temperature 40-45 ^{o}C to give the hexane extract (brownish syrup, 129.7 g) and the EtOH extract (dark brownish sticky solid, 281.5 g). The extraction sequence and detailed isolation of compounds **1**-**14** are shown in supplementary material. The structures of the isolated compounds were identified by comparison of the spectroscopic and physical data with the literature values.

The structures shown in Figures 1 and 2 are identified as germacrone (**1**) [14], curzerenone (**2**) [15], isofuranodienone (**3**) [15], furanodienone (**4**) [15], curdione (**5**) [16], neocurdione (**6**) [16], zederone (**7**) [17], curcumenone (**8**) [18], 13-hydroxygermacrone (**9**) [19], zedoarondiol (**10**) [20], 3-hydroxy-5-platyphyllone (**11**) [21], (3*S*)-1,7-bis(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol (**12**) [22], centrolobol (**13**) [23], (3*S*)-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol (**14**) [24].

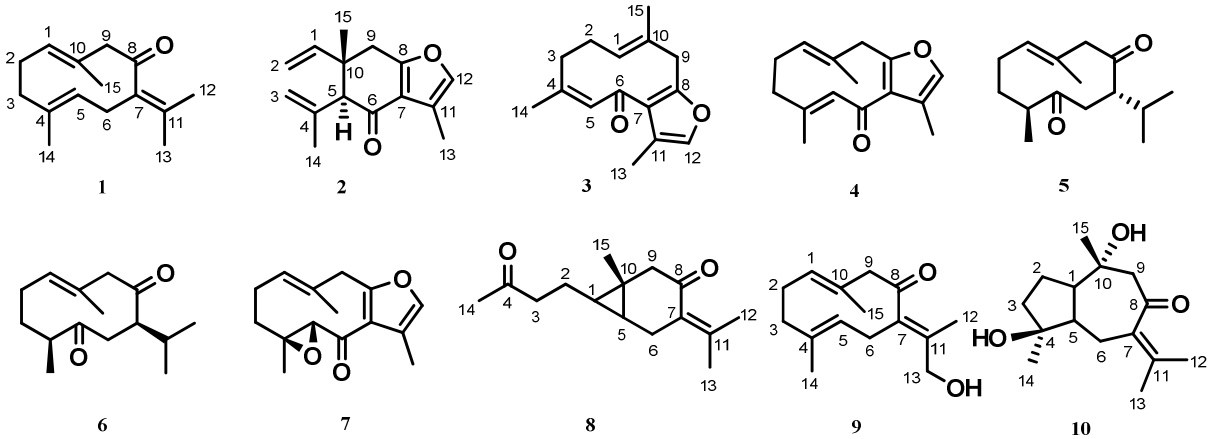

Figure 1. Structures of sesquiterpenoids **1**-**10** isolated from the rhizomes of *C. elata*.

The diarylheptanoids **12** and **13** exhibited the most potent cytotoxic activity against both the KB and NCI-H187 cell lines whereas compound **14** was selectively active against the NCI-H187 cell line. The absence of the keto group at C-5 of the diarylheptanoids seems to increase the cytotoxicity. It should be noted that compounds **12** and **14** were highly active against NCI-H187 cell line; they were only 1.6-fold less active than ellipticine, the reference anticancer drug. The isolated sesquiterpenoids **4** and **9** showed moderately high activity against the NCI-H187 cell line. However, the sesquiterpenoids **1**-**3**,

5-8 and **10**, and the diarylheptanoid **11** were weakly active or inactive against the three cancer cell lines.

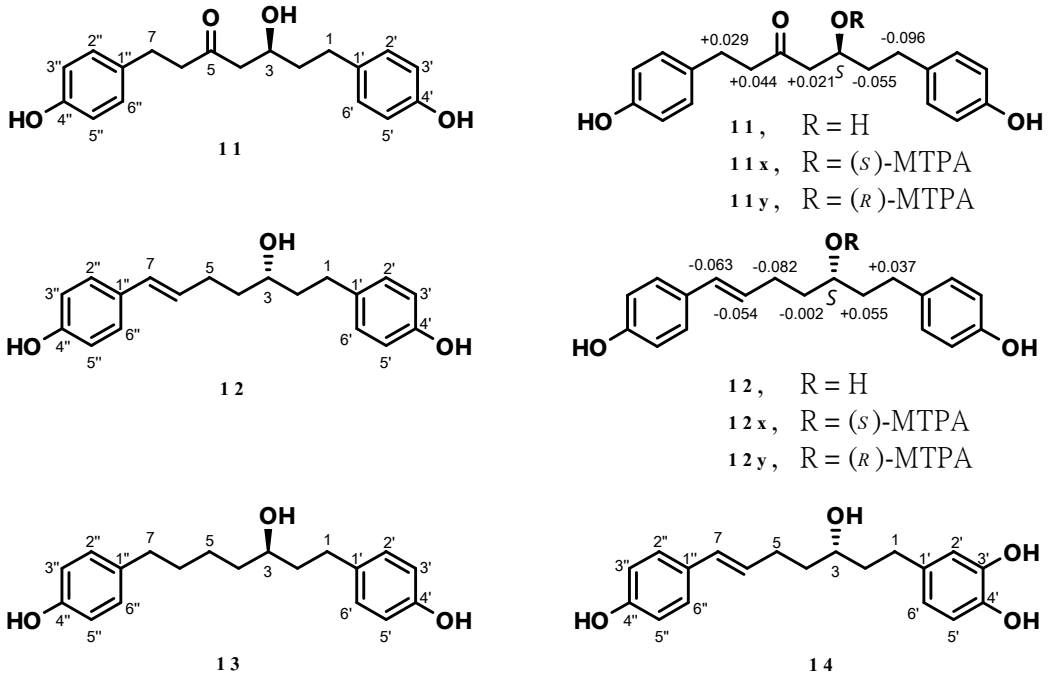

Figure 2. Structures of diarylheptanoids **11-14** isolated from rhizomes of *C. elata*. The absolute configurations of compounds **11** and **12** were determined by the modified Mosher's method through the MTPA esters (**11x** and **11y**, and **12x** and **12y**, respectively).

Table 1. Cytotoxic activity of compounds **1-14**.

Compound	Cytotoxicity (IC_{50}, μM)		
	KB[a]	MCF-7[b]	NCI-H187[c]
1	203.38	202.01	NA[d]
2	NA[d]	114.37	108.64
3	NA[d]	NA[d]	NA[d]
4	101.60	179.05	19.76
5	NA[d]	NA[d]	NA[d]
6	NA[d]	NA[d]	NA[d]
7	201.15	NA[d]	NA[d]
8	NA[d]	NA[d]	64.96
9	82.40	NA[d]	11.10
10	NA[d]	NA[d]	NA[d]
11	50.42	NA[d]	59.24
12	10.09	143.37	4.45
13	4.76	158.54	9.55
14	NA[d]	NA[d]	4.54
Ellipticine	1.81	NT[e]	2.77
Doxorubicin	0.42	0.98	0.06

[a]Human oral epidermoid carcinoma; [b]Human breast cancer cells;
[c]Human small cell lung cancer cells; [d]NA, inactive at > 50 μg/ml.; [e]NT, not tested.

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Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/RNP

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