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Commercially processed dry ginger (*Zingiber officinale*): Composition and effects on LPS-stimulated PGE_2 production

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Abstract

Using techniques previously employed to identify ginger constituents in fresh organically grown Hawaiian white and yellow ginger varieties, partially purified fractions derived from the silica gel column chromatography and HPLC of a methylene chloride extract of commercially processed dry ginger, *Zingiber officinale* Roscoe, Zingiberaceae, which demonstrated remarkable anti-inflammatory activity, were investigated by gas chromatography-mass spectrometry. In all, 115 compounds were identified, 88 with retention times (R_t) >21 min and 27 with <21 min. Of those 88 compounds, 45 were previously reported by us from fresh ginger, 12 are cited elsewhere in the literature and the rest (31) are new: methyl [8]-paradol, methyl [6]-isogingerol, methyl [4]-shogaol, [6]-isoshogaol, two 6-hydroxy-[*n*]-shogaols ($n = 8$ and 10), 6-dehydro-[6]-gingerol, three 5-methoxy-[*n*]-gingerols ($n = 4$, 8 and 10), 3-acetoxy-[4]-gingerdiol, 5-acetoxy-[6]-gingerdiol (stereoisomer), diacetoxy-[8]-gingerdiol, methyl diacetoxy-[8]-gingerdiol, 6-(4′-hydroxy-3′-methoxyphenyl)-2-nonyl-2-hydroxytetrahydropyran, 3-acetoxydihydro-[6]-paradol methyl ether, 1-(4′-hydroxy-3′-methoxyphenyl)-2-nonadecen-1-one and its methyl ether derivative, 1,7-*bis*-(4′-hydroxy-3′-methoxyphenyl)-5-methoxyheptan-3-one, 1,7-bis-(4′-hydroxy-3′-methoxyphenyl)-3-hydroxy-5-acetoxyheptane, acetoxy-3-dihydrodemethoxy-[6]-shogaol, 5-acetoxy-3-deoxy-[6]-gingerol, 1-hydroxy-[6]-paradol, (2*E*)-geranial acetals of [4]- and [6]-gingerdiols, (2*Z*)-neral acetal of [6]-gingerdiol, acetaldehyde acetal of [6]-gingerdiol, 1-(4-hydroxy-3-methoxyphenyl)-2,4-dehydro-6-decanone and the cyclic methyl orthoesters of [6]- and [10]-gingerdiols. Of the 27 $R_t < 21$ min compounds, we had found 5 from fresh ginger, 20 others were found elsewhere in the literature, and two are new: 5-(4′-hydroxy-3′-methoxyphenyl)-pent-2-en-1-al and 5-(4′-hydroxy-3′-methoxyphenyl)-3-hydroxy-1-pentanal. Most of the short R_t compounds are probably formed by thermal degradation during GC (which mimics cooking) and/or commercial drying. The concentrations of gingerols, the major constituents of fresh ginger, were reduced slightly in dry ginger, while the concentrations of shogaols, the major gingerol dehydration products, increased.

Keywords: *Zingiber officinale*; Zingiberaceae; Ginger; Rhizomes; Ginger derivatives

1. Introduction

In our previous report on the gas chromatography-mass spectrometry (GC-MS) analysis of partially purified fractions from two organically grown fresh white and yellow ginger varieties, *Zingiber officinale* Roscoe

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(Zingiberaceae) from Hawaii, we described the identification of 63 compounds including 31 compounds previously reported as ginger constituents, 25 new gingerol derivatives and 7 thermal degradation products of gingerols (Jolad et al., 2004). In this paper we report similar findings from the GC-MS analysis of biologically active column chromatography (CC) fractions from the CH_2Cl_2 extract of commercially processed dry ginger powder with special emphasis on their activity in inhibiting in vitro PGE_2 production.

Chronic inflammation has been associated with a number of human diseases including chronic obstructive pulmonary disease, asthma and rheumatoid arthritis. While "conventional" treatments have met with some success, patients suffering from diseases with associated chronic inflammation are turning to alternatives for relief of their symptoms or as prophylactic treatments. These alternatives include dietary supplements that are purported to have anti-inflammatory actions. However, the efficacy and potency of these supplements have not been studied in great detail. Plants (or supplements derived from the plants) that have received attention as being useful for chronic inflammation include ginger.

Inflammation is associated with a large range of mediators that initiate the inflammatory response, recruit and activate other cells to the site of inflammation and subsequently resolve the inflammation (Gallin and Snyderman, 1999). In general, the chemical mediators can be divided into two large classes: cytotoxins and arachidonic acid metabolites. Products produced by the metabolism of arachidonic acid include both cyclooxygenase products (prostaglandins, thromboxanes) and lipooxygenase products (leukotrienes). Products such as LTB4 and PGE_2 that are representative of these two pathways can initiate polymorphonuclear (PMN) leukocytes recruitment and changes in vascular tone and blood flow. Increased production of prostaglandins during an inflammatory response is achieved by induction of cyclooxygenase 2 (COX-2).

Several studies have indicated that compounds found in ginger are effective in relief of symptoms from chronic inflammatory diseases. Administration of ginger has resulted in patients relating decreased symptoms of rheumatoid arthritis (Srivastava and Mustafa, 1992). Gingerol (a major component of ginger) has been reported to have anti-inflammatory actions. For gingerol these include suppression of both cyclooxygenase and lipooxygenase metabolites and arachidonic acid (Kiuchi et al., 1992; Srivas, 1984; Tjendraputra et al., 2001). Our own research has found that organic extracts from ginger rhizomes or standards containing gingerols were able to inhibit LPS-induced PGE_2 ($IC50 < 0.1$ μg/ml) production in U937 cells. Extracts containing either predominantly gingerols or shogaols (identified by HPLC) were both highly active at inhibiting LPS-induced PGE_2 production ($IC50 < 0.1$ μg/ml), while extracts that contained unknown compounds were less effective ($IC_{50} < 3.2$ μg/ml). Extracts or standards containing predominantly gingerols were capable of inhibiting COX-2 expression while shogaol containing extracts had no effect on COX-2 expression (Lantz et al., 2005).

2. Results and discussion

Of the 10 final CC fractions analyzed for biological activity (Table 1), the initial two lipophilic fractions (X/1 and X/2) and the final polar fractions (X/9 and X/10), representing 9.0 (22.5%) and 11.2 g (28%), respectively, of the isolate, had insignificant activity and were, therefore, excluded from further analysis. The remaining six fractions (X/3–8), which exhibited

Table 1
Summary of column chromatography fractionation profile of CH_2Cl_2 extract (X, 40 g) of commercial dry ginger powder

Extract/fraction	Yield (g)	PGE_2 IC_{50} (μg/ml)	Cytotoxic dose (μg/ml)	Compounds detected
Fresh white ginger	–	0.051	10	Original
Fresh yellow ginger	–	0.072	50	Original
Dry ginger (X)	–	0.055	50	Original
X/1	8.96	0.411	50	[a]
X/2	0.06	0.255	>50	[a]
X/3	8.68	0.052	0.1	**1, 3–5, 9, 15, 19, 20, 22, 25, 26, 28–32, 34, 62, 63, 77, 78**
X/4	1.72	0.060	50	**10, 15, 16, 19, 20, 25, 36, 51, 54, 55, 59**
X/5	2.11	0.053	50	**9, 11, 19, 22, 25, 26, 36**
X/6	5.96	0.053	50	**9, 11, 18, 22, 25**
X/7	0.69	0.064	5	**6, 9, 19, 25, 49, 51, 65, 85**
X/8	0.70	0.060	50	**9, 18–20, 22, 25, 27, 43–45, 65, 70, 71, 86, 87**
X/9	4.77	0.430	50	[a]
X/10	6.44	25.388	50	[a]

Fractions (X/1–10), yields, activity in inhibiting in vitro PGE_2 production and compounds detected by GC-MS in the active fractions.
In vitro PGE_2 assay data for two fresh ginger extracts are included in the table for comparison.
[a] Not subjected to GC-MS analysis.