A new lignan from the stem bark of Fagraea fragrans Roxb

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Regular Article

Syntheses of all stereoisomers of aptosimon (9-oxosesamin) and their effects on plant growth regulation and diacylglycerol acyltransferase inhibition

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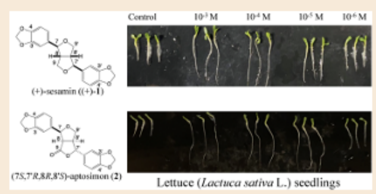
Supplementary material

All eight stereoisomers of aptosimon (9-oxosesamin) were synthesized by employing Evans' *anti*- and *syn*-aldol condensations. Among them, the (7*S*,7′*R*,8*R*,8′*S*)-aptosimon was more active than (+)- and (−)-sesamin at 1×10^{-5} M in promoting lettuce root growth under illumination conditions (44 μmol·m^{-2}·s^{-1}). The effect of the 9-oxo group on the promotion of lettuce root growth was not observed from the results of activity experiments of stereoisomers carrying the same stereochemistry as those of (+)- and (−)-sesamin (**1**). However, the importance of 7*S*-configurations of aptosimon (9-oxosesamin) stereoisomers for the higher promotion of lettuce root growth was suggested. Based on optical rotation data and NMR analysis of the synthesized stereoisomers, the diacylglycerol acyltransferase inhibitory aptosimon was determined to be (7*S*,7′*S*,8*S*,8′*R*)-aptosimon and its enantiomer.



Keywords: lignan, aptosimon, sesamin, stereochemistry, plant growth regulation.

Introduction

To explore the biological activity of natural compounds, it is important to synthesize and analyze their stereoisomers. The chemical data obtained from the synthetic stereoisomers are useful to determine the stereochemistry of biosynthesized compounds. Furthermore, biological experiments using the stereoisomers would provide information on the stereochemistry-activity relationship. In this experiment, we synthesized aptosimon[1)] stereoisomers **2**, **3**, *ent*-**2**, *ent*-**3**, **4**, **5**, *ent*-**4**, and *ent*-**5** of the 9-furofuranone lignan[2)] (9-oxosesamin) (Fig. 1) and determined their effect on seedling growth.

(+)- and (−)-Sesamin[1)] are plant growth regulatory compounds.[3,4)] Since furofuran lignan with carbonyl group at the 9-position is biosynthesized by plants,[2)] it is of interest to understand its importance on plant growth. The isolation of 9-furofuranones[5–10)] including aptosimon is in progress by many research groups. Although 9-furofuranones on biological activities[11–13)] and their syntheses[14–16)] have been reported, the effect of stereochemistry on biological activity remains to be clarified. The success of our synthetic study of aptosimon stereoisomers would facilitate further biological research. In phytochemical research, such synthesis would make the comparison of aptosimon stereoisomers with other plant growth regulatory lignans[17–27)] for their effects on plant growth possible. Understanding the effect of aptosimon stereochemistry on plant growth may provide information for developing novel regulatory compounds based on the furofuran lignan structure. Furthermore, the chemical data of the synthetic stereoisomers in this research could help determine the stereochemistry of the diacylglycerol acyltransferase (DGAT) inhibitor in *Eleutherococcus senticosus*.[12)]

The synthetic strategy to obtain all stereoisomers of aptosimon is illustrated in Scheme 1. Evans' respective *anti*- and *syn*-aldol condensation products **6**[28)] and 2′-*epi*-**6**[29)] were selected

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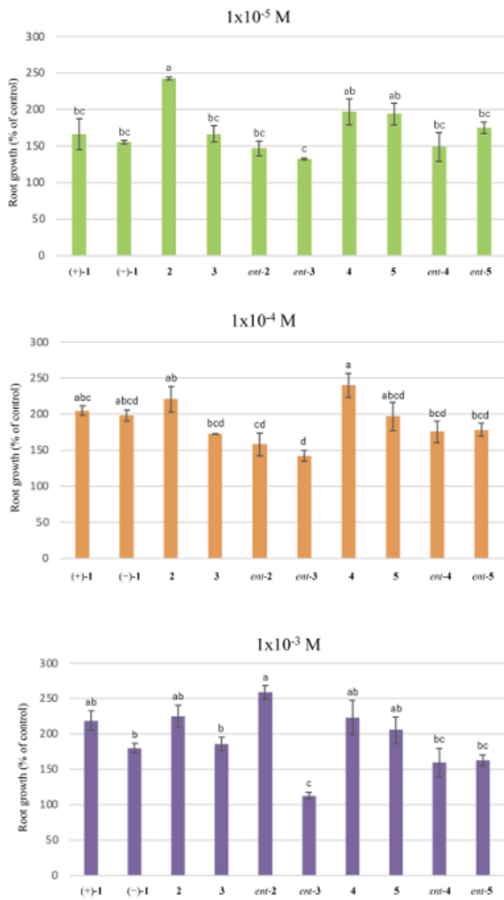

Fig. 3. Effects of (+)-, (−)-sesamin ((+)-**1**, (−)-**1**), and all stereoisomers of aptosimon (**2**–**5**, *ent*-**2**–*ent*-**5**) on lettuce root growth at 1×10^{-5}, 1×10^{-4}, 1×10^{-3} M (100%: same as control, more than 100%: root growth promotion, 25°C under illumination, 44 μmol·m^{-2}·s^{-1}, one-way ANOVA, Tukey post-test, $p<0.05$. a, b, c, d: The same letters between different bars do not show significant difference, on the other hand, the different letters between different bars show significant difference).

DGAT inhibitor[12] of *E. senticosus* was an enantiomeric mixture of **4** and *ent*-**4**. In the plant growth experiment, the stereoisomer **2** was more potent stereoisomer than (+)- and (−)-sesamin (**1**) for lettuce root growth at 1×10^{-5} M. The importance of 7*S*-configurations of aptosimon (9-oxosesamin) stereoisomers for the higher promoting lettuce root growth was suggested. This discovery contributes to phytochemical research and could lead to the development of a novel plant growth regulatory compound.

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Electronic supplementary materials

The online version of this article contains supplementary material, which is available at https://www.jstage.jst.go.jp/browse/jpestics/.

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Phytochemical Analysis and Bioactivity Evaluation of Ethanolic Exctract of Ironwood (*Fagraea fragrans* Roxb.) Leaves

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Abstract

Ironwood (*Fagraea fragrans* Roxb.) has been widely used by the community as a medicinal plant, as well as a cosmetic ingredient. Various parts of the ironwood plant are used for health due to the content of metabolite compounds such as alkaloids, steroids, saponins, quinones, and tannins. In an effort to determine the bioactive metabolite compounds, an analysis was carried out on the ethanol extract of Ironwood leaves using GC-MS. The analysis revealed 131 peaks, with 79 corresponding to identified compounds. Five principal dominant compounds were identified: cis-13-Octadecenoic acid, 5-Hydroxymethylfurfural, n-Hexadecanoic acid, Erythocentaurin, and 5-Benzofuranacetic acid. Most of the metabolite compounds in Ironwood leaves exhibit bioactivity as antioxidants, antimicrobials (antibacterial, antifungal), antivirals, anti-inflammatory, anticancer, antiandrogens, antidiabetics, and other bioactivities. Based on the metabolite compounds and bioactivity, ironwood leaves have great potential to be developed as a source of medicinal and cosmetic ingredients.

Keywords: Phytochemical; *Fagraea fragrans* Roxb.; Tembesu; Antioxidant; Bioactivity; 5-Hydromethylfurfural.

INTRODUCTION

Ironwood plant (*Fagraea fragrans* Roxb.) belongs to the Gentianaceae family and is known as *Tembesu* in Indonesia, which is a timber-producing plant. Ironwood has been widely used by the community as a traditional medicinal plant. The use of Ironwood as medicine starts from the roots, leaves, bark, and flowers to fruit (Wahyudi *et al*., 2022), and Basir *et al*. (2020) utilize the fruit for cosmetic ingredients. The various parts of Ironwood, including its fruit, stem, and leaves, are used for their anti-inflammatory, antimicrobial, anticancer, and antioxidant properties (Sari et al., 2023). The leaves relieve itching caused by eczema or allergies (Komalasari *et al*., 2018). The content of Ironwood leaf extract shows antibacterial, anti-inflammatory, antifungal, and antioxidant activities (Rattanaburi *et al*., 2020).

The considerable utilization of ironwood leaves is due to the content of metabolites that function as active ingredients, which are also diverse. According to Wahyudi *et al*. (2022), the active compounds terpenes, flavonoids, and phenols have strong antioxidant activity. Furthermore, Rattanaburi *et al*. (2020) stated that the metabolite compounds of ironwood leaves also contain alkaloids, steroids, saponins, quinones, and tannins. Furthermore, Basir *et al*. (2020) reported metabolite analysis with LC-MS on methanol extract; Ironwood fruit detected 14 compounds including *4-(2-hydroxyethyl)-5-vinyl nicotinic acid lactone* (gentianin). Gentianin is reported to have anti-inflammatory, analgesic, antihistamine, anticonvulsant, hypotensive, antipsychotic, sedative, diuretic, antimalarial, antiamoebic, antibacterial, and antimutagenic properties. In addition to gentianin, there are also other unique compounds, namely *ginsenoside ro methyl ester*, with bioactivity as anti-aging, anti-diabetic activity, immunoregulatory activity, anti-cancer activity, and neuroregulatory activity.

In exploring the bioprospection of metabolites in ironwood, it is necessary to analyze the non-target metabolomic approach with GC-MS to phytochemical analysis in ethanol extracts of Ironwood leaves and trace the bioactivity of these compounds. This research is expected to be useful in efforts to develop the potential, especially the ironwood leaf part, for herbal medicinal and cosmetic ingredients.

MATERIALS AND METHODS

Plant Materials

Ironwood leaf samples were collected from the Sriwijaya University Campus, located in North Indralaya, Ogan

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