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# α-Glucosidase inhibitors from the seeds of *Syagrus romanzoffiana*

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**Abstract**

Bioassay-guided fractionation against α-glucosidase resulted in isolation and characterization of eight active compounds from the EtOH extract of the seeds of *Syagrus romanzoffiana*. Of these, seven are stilbenoids, and two of them, 13-hydroxykompasinol A (**1**) and scirpusin C (**4**), possess potent inhibitory activity against α-glucosidase type IV from *Bacillus stearothermophilus* with the $IC_{50}$ value of 6.5 and 4.9 μM, respectively. The *in vivo* assay on normal Wistar rats using oral sucrose challenge also demonstrated that kompasinol A (**2**) and 3,3′,4,5,5′-pentahydroxy-*trans*-stilbene (**5**) possess significant effect in reducing the postprandial blood glucose level (10.2% and 12.1% at 10 mg/kg, respectively). These results suggest that stilbenoids might be explored for their therapeutic potential as hypoglycemic agents.


*Keywords:* *Syagrus romanzoffiana*; Arecaceae; α-Glucosidase inhibitor; Stilbenoids; 13-Hydroxykompasinol A; Scirpusin C; Type 2 diabetes

## 1. Introduction

The worldwide estimation of diabetic patients around 2030 will be more than double from that of 2005, and most of these will be dominated by those suffering from type 2 diabetes (Gershell, 2005). This increasing trend in type 2 diabetes mellitus has become a serious medical concern worldwide that prompts every effort in exploring for new therapeutic agents to stem its progress. Although the drug treatment for type 2 diabetes mellitus has been improved to some extent during the last decade, drug resistance is still a big concern that needs to be dealt with effective approaches. Thus, the pursuit of drugs acting on an unique target, which is also devoid of the tolerance problem is always the ideal aim of researchers. α-Glucosidase inhibitors act against the enzyme in the gut that restrains liberation of glucose from oligosaccharides and thereby reduces the postprandial glucose levels and insulin responses (Casirola and Ferraris, 2006). Such inhibitors, including acarbose and voglibose, are currently used clinically in combination with either diet or other anti-diabetic agents to control blood glucose levels of patients (Van de Laar et al., 2005). To either avoid or decrease the adverse effects of current agents and also to provide more candidates of drug choices, it is still necessary to search for new α-glucosidase inhibitors for further drug development. Natural resources provide a huge and highly diversified chemical bank from which we can explore for potential therapeutic agents by bioactivity-targeted screenings. Thus, we had tried to use bioassay guided approach to find active ingredients from Formosan plants. From preliminary tests, we found that several plant extracts were active against this specific enzyme and among them the defatted EtOH extract of the seeds of *Syagrus romanzoffiana* (Cham.) Glassman (Arecaceae) exhibited potent activity against α-glucosidase type IV from *Bacillus stearothermophilus* ($IC_{50} < 10$ μg/ml). This plant, known as queen palm, is a common and familiar sight in streets, gardens and parks in either subtropical or tropical landscapes. The gum exudate of this plant had

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been found to contain a heteropolysaccharide composed of fucose, arabinose, xylose galactose, glucose and uronic acid (Simas et al., 2006). A few components such as flavonoids and steroids had been isolated from its dried leaves (Idaka et al., 1991; EI-Sakhway, 1998). This plant was also demonstrated to possess hypoglycemic effect and cytotoxic activity (EI-Sakhway, 1998). We followed the fractionation by *in vitro* bioassay against α-glucosidase to isolate active ingredients from this plant. Two of the major active compounds isolated were tested for their hypoglycemic effect on oral sucrose challenged rat model. The followings describe the outcome of these efforts.

## 2. Results and discussion

Bioassay guided screening indicated that the defatted EtOH extract of the seeds of *S. romanzoffiana* showed 55% inhibitory activity against α-glucosidase at a concentration of 10 μg/ml. Further fractionation indicated the active ingredients to be concentrated in the BuOH soluble fraction, having 73% inhibition at 10 μg/ml level. This fraction was further separated over Sephadex LH-20 and low pressure RP-18 columns that eventually yielded eight active compounds (**1**–**8**). Compounds **5**–**7** were characterized as the known 3,3′,4,5,5′-pentahydroxy-*trans*-stilbene, piceatannol, and resveratrol, respectively, by NMR spectroscopic comparisons (Nakajima et al., 1978). Compound **8** was identified as 4-hydroxybenzoic acid (Scott, 1972).

The $^1$H NMR spectra of compounds **1** (Table 1) and **2** (Table S1) were very similar, both containing characteristic signals for a 2,6-disubstituted-7,8-benzo-3-oxabicyclo-[3.3.0]octane moiety, and common signals for four aryl protons, appearing as a two-proton singlet and an AX system. The presence of a 2,6-disubstituted-7,8-benzo-3-oxabicyclo[3.3.0]octane moiety was confirmed by the analysis of a COSY spectrum of **1**, displaying the following correlations: $\delta$ 4.59 (*d*, H-8) ↔ $\delta$ 3.75 (*dd*, H-7) ↔ $\delta$ 3.01 (*dq*, H-8′) ↔ $\delta$ 4.12 (*d*, H-7′), 4.45 (*t*, H-9′β) and 3.52 (*t*, H-9′α), and $\delta$ 4.45 ↔ $\delta$ 3.52. Compound **2** was identified as kompasinol A (Kulesh et al., 1995; Kobayashi et al., 1996), based on comparison of the spectroscopic data and the optically inactive property. The $^1$H NMR spectrum of **1** (Table 1) was slightly different from that of **2** (Table S1) by replacing an ABX system ($\delta$ 6.85, *d*, $J = 1.6$ Hz; 6.76, *d*, $J = 8.0$ Hz; and 6.73, *dd*, $J = 8.0$, 1.6 Hz) in that of **2** with a two-proton singlet ($\delta$ 6.42). The molecular formula of **1**, $C_{25}H_{24}O_9$, as deduced from HR-FAB-MS, had one additional oxygen atom relative to that of **2**. Pooling these $^1$H NMR and MS data together would allow characteriza-

Table 1
$^1$H and $^{13}$C NMR, and HMBC spectroscopic data for compounds **1** and **4** ($CD_3OD$, 400 MHz)

| Position | **1** | | | **4** | | |
|---|---|---|---|---|---|---|
| | $\delta_H$ | $\delta_C$ | HMBC (H → C) | $\delta_H$ | $\delta_C$ | HMBC (H → C) |
| 1 | | 148.6 *s* | | | 141.1 *s* | |
| 2 | | 123.0 *s* | | 6.19 *d* (2.1) | 105.8 *d* | 1, 3, 4, 6, 7 |
| 3 | | 156.3 *s* | | | 159.4 *s* | |
| 4 | 6.18 *d* (2.0) | 102.9 *d* | 2, 3, 5, 6 | 6.09 *t* (2.1) | 102.3 *d* | 2, 3, 5, 6 |
| 5 | | 160.1 *s* | | | 159.4 *s* | |
| 6 | 6.25 *d* (2.0) | 103.3 *d* | 2, 4 | 6.19 *d* (2.1) | 105.8 *d* | 1, 2, 4, 5, 7 |
| 7 | 3.75 *dd* (8.8, 4.4) | 59.7 *d* | 2, 9, 9′ | 6.57 *d* (16.2) | 128.4 *d* | 1, 2, 6, 9 |
| 8 | 4.59 *d* (4.4) | 89.4 *d* | 1, 7, 8′, 9, 9′, 10, 14, | 6.62 *d* (16.2) | 126.5 *d* | 1, 9, 10, 14 |
| 9 | | 134.6 *s* | | | 126.6 *s* | |
| 10 | 6.42 *s* | 106.4 *d* | 8, 11, 12, 14 | | 121.4 *s* | |
| 11 | | 147.1 *s* | | | 149.6 *s* | |
| 12 | | 133.7 *s* | | | 130.4 *s* | |
| 13 | | 147.1 *s* | | | 147.8 *s* | |
| 14 | 6.42 *s* | 106.4 *d* | 8, 10, 12, 13 | 6.69 *s* | 105.6 *d* | 8, 10, 12, 13 |
| 1′ | | 137.9 *s* | | | 134.4 *s* | |
| 2′ | 6.31 *s* | 105.5 *d* | 1′, 3′, 4′, 7′ | 6.37 *s* | 105.7 *d* | 1′, 3′, 4′, 7′ |
| 3′ | | 149.1 *s* | | | 147.0 *s* | |
| 4′ | | 134.7 *s* | | | 134.1 *s* | |
| 5′ | | 149.1 *s* | | | 147.0 *s* | |
| 6′ | 6.31 *s* | 105.5 *d* | 1′, 4′, 5′, 7′ | 6.37 *s* | 105.7 *d* | 1′, 4′, 5′, 7′ |
| 7′ | 4.12 *d* (0.8) | 52.1 *d* | 1, 1′, 2, 2′, 3, 6′, 7, 8′, 9′ | 5.26 *d* (5.3) | 95.4 *d* | 10, 11, 1′, 2′, 6′, 8′, 9′ |
| 8′ | 3.01 *dq* (0.8, 8.8) | 56.5 *d* | 1, 2, 1′ | 4.39 *d* (5.3) | 58.7 *d* | 10, 11, 1′, 7′, 9′, 10′, 14′ |
| 9′ | 3.52 *t* (8.5) (α) | 75.0 *t* | 7′ | | 147.6 *s* | |
| | 4.45 *t* (8.5) (β) | | 7, 8 | | | |
| 10′ | | | | 6.16 *d* (1.8) | 107.3 *d* | 8′, 11′, 12′ |
| 11′ | | | | | 159.8 *s* | |
| 12′ | | | | 6.17 *t*-like | 102.7 *d* | 10′, 11′, 12′, 13′ |
| 13′ | | | | | 159.8 *s* | |
| 14′ | | | | 6.16 *d* (1.8) | 107.3 *d* | 8′, 12′, 13′ |
| $OCH_3$ | 3.72 *s* | 56.7 *q* | 3′, 5′ | | | |