<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Red pigment from Saw Palmetto: a natural product for potential alternative cancer treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>Feng, Y; Okuda, S; Tan, HY; Wang, N; Tsao, SW; Takahashi, M</td>
</tr>
<tr>
<td><strong>Citation</strong></td>
<td>The 2015 EACR-AACR-SIC Special Conference, Florence, Italy, 20-23 June 2015.</td>
</tr>
<tr>
<td><strong>Issued Date</strong></td>
<td>2015</td>
</tr>
<tr>
<td><strong>URL</strong></td>
<td><a href="http://hdl.handle.net/10722/233106">http://hdl.handle.net/10722/233106</a></td>
</tr>
<tr>
<td><strong>Rights</strong></td>
<td>This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.</td>
</tr>
</tbody>
</table>
Red pigment from Saw palmetto: 
A natural product for potential alternative cancer treatment

Yibin Feng1*, Sari Okuda2, Hor Yue Tan1, Ning Wang1, Sai-Wah Tsao3, Masao Takahashi2

1 School of Chinese Medicine, LKS Faculty of Medicine, The University of Hong Kong (*Corresponding author).
2 Heimat Co., Ltd. Heimat Building, 1-21-3 Nihonbashi, Chuo-Ku, Tokyo, Japan.
3 Department of Anatomy, Center of Cancer research, LKS Faculty of Medicine, The University of Hong Kong.

**Introduction**

Saw palmetto is extract of the fruit of Serenoa repens (Bartram J.K.Small, an edible plant originated from the Southeastern United States. It has been used in traditional, complementary and alternative medicine as a tonic, expectorant and antiseptic for treatment of various illnesses, especially urinary and reproductive system problems. Approximately 90% of Saw palmetto containing fatty acids and has been claimed for its therapeutic effect on benign prostatic hyperplasia (BPH). Previous studies also suggested the in vitro and in vivo anti-cancer effect of lipidosterolic extract of Saw Palmetto. However, recent epidemiology and randomized trials showed that there is no association of prostate cancer risk between the intervention and placebo group. Although there exists discrepancy between the studies on cancer prevention of Saw palmetto, we couldn’t exclude the potential anti-tumor effect of Saw palmetto on other tumor models. In current study, the anti-tumor effect of a small proportion of natural pigment compounds isolated from the commercial Saw Palmetto Extract were investigated. To date, there is no previous study reported on any bioactivity of these pigmented compounds from Saw Palmetto.

**Results**

**NYGs significantly exhibited anti-tumour effect in HCC xenograft model.**

To investigate the effect of NYGs on tumour growth in vivo, the MHCC97L xenograft mice were administrated with three products of NYGs, namely NYG-1, NYG-4, and NYG-7 in two doses (5mg/kg and 10mg/kg every 2 days, intra-peritoneal) for 4 weeks and doxorubicin served as control. After 4 weeks of NYGs administration, the body weight of NYGs administrated mice remained unchanged while significant weight loss observed in doxorubicin treated mice (results not shown), indicating that NYGs have minimal toxicity to the animal at both doses. A significant regression in tumour size was observed in NYGs treated mice in comparison to control and the effect is in dose-dependent manner. There is at least two-point five fold of tumour size reduction across the treatment groups. As for NYG-1, it showed the most marked tumour inhibitory effect in comparison to other treatment group and 10mg/kg of NYG-1 exhibited as potent effect as doxorubicin-treated group of mice.

![Figure 1. NYGs induced tumour regression on HCC xenograft model.](image)

NYGs has no cytotoxic effect on HCC cell lines, but it inhibited cancer growth in in vitro model and blood formation suggesting that NYGs may be used for alternative cancer treatment by inhibiting tumor neovascularization. The study was supported by grants from the University of Hong Kong (Project code: 104002889 and 104003422), Wong’s Donation (Project code: 207040314) and Hong Kong Government Matching Funding (Project code: 207060411).

**Conclusion**

NYGs is neither cytotoxic against cancer cells nor normal cells. Next, the in vitro cytotoxic effect of NYGs to HCC cell line, MHCC97L and normal hepatic cell line, L-02 was examined via MTT assay. The cytotoxicity of NYGs-treated MHCC97L and L-02 cells were determined after 48 hours of incubation (Fig. 2). NYGs exerted no cytotoxicity effect against MHCC97L and L-02 up to 1000μg/ml, suggesting NYGs exerted minimal cytotoxic effect towards normal and cancerous cell lines. Based on the in vivo results, the most potent NYGs, NYG-1 was employed for further experiments. To evaluate the effect of NYG-1 on the expression of VEGF in HCC cell, MHCC97L cells supernatant was subjected to ELISA after exposure to NYG-1 for 48 hours. Results showed no significant reduction of secretory VEGF protein by NYG-1 (Fig. 3). We also further examined whether NYG-1 has any effect on VEGFR mRNA expression, yet quantitative PCR analysis showed NYG-1 has least effect on mRNA expression of VEGFR. These results indicated that the anti-tumour effect of NYG-1 is independent to the activity on HCC cells.

![Figure 2. No significant cytotoxicity on MHCC97L and L-02 cells.](image)

NYG-1 blocked migration and tube formation ability of HUVECs. We further explored the effect of NYG-1 on HUVEC cells. HUVEC cells were either exposed to VEGF alone or in combination with NYG-1. Using migration chamber assay, we observed the blocked migratory ability of HUVECs across the chamber after treatment with NYG-1 in dose dependent manner. Besides, the tube formation ability of HUVECs was attenuated after NYG-1 intervention, further suggested the functions of HUVECs was abolished in the presence of NYG-1 (Fig. 4). This results indicate the anti-tumour effect of NYGs may be attributed by its inhibitory effect on endothelial cells.

![Figure 3. No significant changes of VEGF and VEGFR expression.](image)

![Figure 4. NYG-1 blocked (A) migration and (B) tube formation ability of HUVECs.](image)