Studies on “Dragon Blood”

Dragon blood is one of the components used in “Jinchuang ointment”. It has been used as a folk remedy for wounds, inflammation, and dysfunctional blood circulation worldwide for more than a thousand years. This deep-red resin based medicine can be produced from several entirely different plants in traditional Chinese market. Historically, *Dracaena cinnabari* in Socotra Island, Yemen (Fig. 1A and 1B) was the first plant species used as a medicinal source of dragon blood. Since this plant is an endangered endemic species, dragon blood obtained from the palm tree, *Daemonorops draco*, in southeast Asia, became the major product used in the traditional Chinese medicine market after the Ming dynasty between 1368 AD and 1644 AD (Fig. 1D and 1E). More recently, native dragon blood tree in China, *Dracaena cochinchinensis*, was found by a famous botanist, Professor Cai Xi-Tao, in 1972. (Fig. 1C)

Figure 1. (A) and (B) Dragon blood tree, *Dracaena cinnabari*, on Socotra Island, Yemen; (C) Dragon blood tree, *Dracaena cochinchinensis*, in Kunming botanical garden, Yunnan Province, China; (D) and (E) Palm tree, *Daemonorops draco*, on Sumatera Island, Indonesia. [1]

In current traditional Chinese medicine markets, palm tree “dragon blood” is the mainstream product. It can be classified into two different categories by its appearance, powder form and block form. The powder form is a dried powder obtained from the red fruit resin of the palm tree, *Daemonorops draco*, without other artificial additives (Fig. 2E and 2F). On the other hand, the block form dragon blood

is a dark brown sub-globular block with a diameter of 6-8 cm (Fig. 2A-2D). For the purpose of transport and storage, the powder from fruit resin is mixed with an excipient, dammar gum, to obtain the solid. It is generally believed that dammar gum protects the active compounds inside the block from moisture and oxygen, extending the shelf life of the product. The extended shelf life of the block form may be why it is the main retail product sold in the traditional Chinese medicine market.

However, dragon blood products from *Dracaena cochinchinensis* or *Dracaena cinnabari* are still can be found. A matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) based method for rapid screening of dracorhodin in commercial dragon blood samples was established by our group. In contrast to MALDI-TOF, LC-MS is a time-consuming and costly-consumptive method, not ideal for routine and large-scale screening of commercial samples. [1]

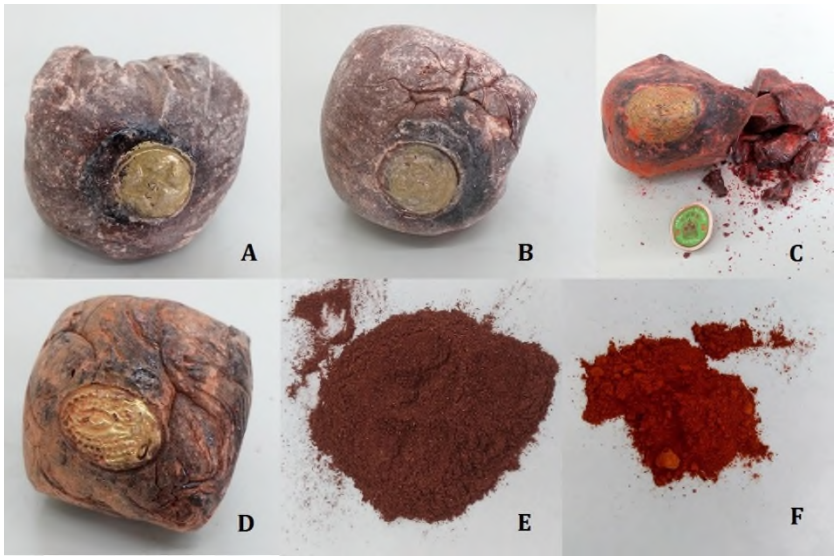

Figure 2. Appearance of powder form and block form dragon blood. Block form dragon blood is made by mixing red tree resin with dammar gum. Block form dragon blood (Sample A, B, C, and D). Powder form dragon blood (Sample E, and F). [2]

Dracorhodin, the active component of dragon blood, is a characteristic compound of the palm tree, *Daemonorops draco*. At present, the only method to evaluate the quality of commercial dragon blood samples is to determine the amount of dracorhodin in a dragon blood sample by HPLC. We used zebrafish embryos as a platform to demonstrate the *in vivo* pro-angiogenic activity of dracorhodin perchlorate, the chemically synthesized analog of dracorhodin (Figure 3). [2] This *in vivo* activity assay method complements the current HPLC-based assay method. In addition, our

results also showed that dracorhodin perchlorate did not induce cell proliferation, but promoted cell migration in HaCaT cells. [3] The use of dragon blood in wound treatment has been recorded in many ancient traditional Chinese medical books. This result shows that dragon blood might play an important role in angiogenesis during wound healing process.

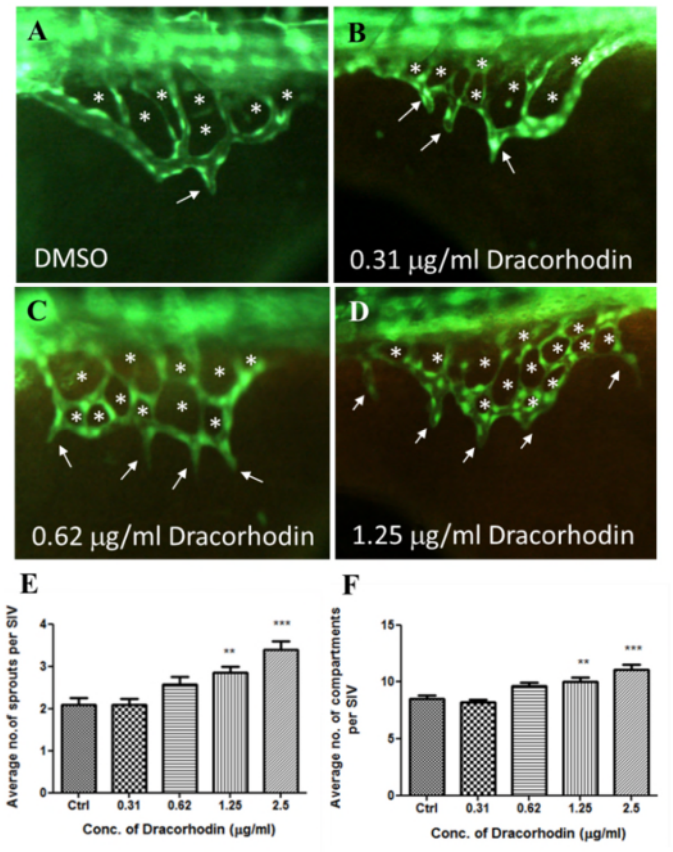

Figure 3. Effect of Dracorhodin perchlorate on sub-intestinal veins of zebrafish embryos.

Sub-intestinal veins (SIV) of control embryo treated with 0.1% DMSO. (A-D) SIV of 72 hpf zebrafish embryos treated with (B) 0.31, (C) 0.62, and (D) 1.25 µg/ml of dracorhodin perchlorate (DP). White arrows indicate extra sprouts. (E) Quantification of average sprout numbers. DP increased the average sprout number in a dose-dependent manner between 0.31 and 1.25 and plateaued at 1.25 to 2.5 µg/ml. (F) Quantification of relative fold changes in sprout length with respect to controls. DP increases the sprout length in a dose-dependent manner. Data is expressed as a mean ± SEM from three independent experiments. Asterisks indicates $P<0.05$ compared with the control group. [2]

Our publication:

1. Wu C, Cai XQ, Chang Y, Chen CH, Ho TJ, Lai SC, Chen HP. "Rapid Identification of Dragon Blood Samples from *Daemonorops draco*, *Dracaena cinnabari* and *Dracaena cochinchinensis* by MALDI-TOF Mass Spectrometry." (2019) *Phytochemical Analysis* **30**, 720-726. (DOI:10.1002/pca.2852).

2. Krishnaraj P, Chang Y, Ho TJ, Lu NC, Lin MD, Chen HP. "*In vivo* Pro-Angiogenic Effects of Dracorhodin Perchlorate in Zebrafish Embryos: A Novel Bioactivity Evaluation Platform for Commercial Dragon Blood Samples."(2019) *Journal of Food and Drug Analysis* **27**, 259-265.
3. Lu CC, Yang CC, Chiu YJ, Tsai FJ, Hsu YM, Yin MC, Juan YN, Ho TJ, Chen HP. "Dracorhodin Perchlorate Enhances Wound Healing via β-catenin, ERK/p38 and AKT Signaling in Human HaCaT Keratinocytes." (2021) *Experimental and Therapeutic Medicine* **22**, 822.