## **Abstract of Presentation**

Biofunctional Molecules from Several Egyptian Herbal Medicines – Black Cumin, Colocynth, Black Pepper –

Hisashi Matsuda and Masayuki Yoshikawa

Kyoto Pharmaceutical University

<u>Abstract</u>: In Egypt, many medicinal plants have been used for the prevention and treatment of various diseases since ancient times. However, in most cases, their effective constituents as well as the mechanisms of action remain uncharacterized. In the course of our study on traditional Egyptian medicines, various new and known bioactive compounds were elucidated. In this paper, we describe the lipid metabolism-promoting, anti-allergic, cytotoxic, and hepatoprotective constituents of *Nigella sativa* (seeds), *Citrullus colocynthis* (fruit), and *Piper nigrum* (fruit).

*Nigella sativa*: The methanolic extract from the seeds of *N. sativa* showed a promotion of lipid metabolism in primary-cultured mouse hepatocytes, suggesting that anti-hyperlipidemic effect and inhibitory effect on fatty liver are expected. By bioassay-guided separation, ten new dolabellane-type diterpenoid alkaloids, nigellamines  $A_1-A_5$ ,  $B_1-B_3$ , C, and D were isolated. Nigellamines  $A_1$ ,  $A_5$ ,  $B_1$ , and  $B_2$  exhibited potent reduction of triglyceride levels in primary-cultured mouse hepatocytes and their activities were equivalent to that of a hypolipidemic agent, clofibrate.

Citrullus colocynthis: The methanolic extract of the fruit of C. colocynthis showed inhibitory effects on ear passive cutaneous anaphylaxis (PCA) reactions as a type I allergic model in mice. From the extract, two new cucurbitane-type triterpene glycosides, colocynthosides A and B, were isolated together with 17 known constituents. cucurbitane-type The principal triterpene glycoside, cucurbitacin E 2-O-B-D-glucopyranoside and its aglycone, cucurbitacin E, significantly inhibited the PCA reactions at 100 and 1.25 mg/kg (p.o.), respectively. Furthermore cucurbitacin E and related aglycones showed potent cytotoxic effects on U937, HL-60, and HT1080 cells, and this effect was suggested to be mediated by an inhibition of cofilin's phosphorylation, at least in part.

**Piper nigrum**: The 80% acetone extracts of the fruit of *P. nigrum* and *P. chaba* exhibited hepatoprotective effects on D-galactosamine (D-GalN)/lipopolysaccharide (LPS)-induced liver injury in mice. Several amide constituents inhibited D-GalN/TNF- $\alpha$ -induced cell death of hepatocytes. Moreover, a principal constituent, piperine, significantly inhibited the D-GalN/LPS-induced liver injury at 5 and 10 mg/kg (*p.o.*), and lowering the TNF- $\alpha$  sensitivity of hepatocytes is involved in the protective effects of piperine.

These findings are useful for chemical and pharmacological elucidation of these natural medicines.