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Anti-cancer Activity of Noni Fruit Juice Against Tumors in Mice

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Abstract of presentation

Noni fruit juice is one of the most popular traditional medicines among native Polynesian islanders in South Pacific Ocean. They use it for diabetes, high blood pressure, cancer, injury, arthritis, digestive distress, arteriosclerosis, pain relief, senility etc. We have confirmed the antitumor potential at animal level that noni fruit juice could inhibit murine tumor growth with a definite curative potential.

The first presentation was in 1992, at the 83rd annual meeting of American Association of Cancer Research at San Diego, CA: Antitumor Activity of *Morinda citrifolia* on Intraperitineally implanted Lewis Lung Carcinoma in Mice (Proc. Am. Soc. Cancer Res. 33, 515, 1992). Then, after two presentations and the brief publication (*Proc. West. Pharmacol. Soc*. 37, 145, 1994 and 39, 7, 1996), we published a full paper in 1999: An immunomodulatory polysaccharide-rich substance from the fruit juice of *Morinda citrifolia* (noni) with antitumour activity (*Phytother. Res*. 13, 380-387, 1999). Now, we have just submitted the second full-paper to *Phytotherapy Research*, entitled " Antitumor potential of a polysaccharide-rich substance from the fruit juice of *Morinda citrifolia* (noni) on sarcoma 180 ascites tumor in mice."

Noni fruit juice is not cytotoxic in cell cultures (Lewis lung carcinoma cell line, Sarcoma 180 cells, human KB carcinoma cell line, or normal NIH/3T3 and BALB/3T3 cell lines), but the juice can indirectly kill the cancer cells via activation of the cellular immune system involving macrophages, natural killer cells and T cells. Therefore, noni fruit juice is one the powerful antitumor immunostimulators of plant food origin without having toxicity.

Antitumor activity of Hawaiian noni fruit juice and the fractions on Lewis lung carcinoma (LLC) in mice

Methods

The syngeneic C57BL/6 mice were inoculated intraperitoneally (i.p.) with LLC (2-4 x 10-5th cells) on day 0. Agent was given i.p. daily or every other day starting on day 1, a total of 4-5 injections.

Results

The original undiluted crude juice (0.1 ml/mouse) showed the clear antitumor activity. It prolonged the mean survival time doubled and the 20-40% of mice cured. The antitumor potential is concentrated into the ethanol-precipitated fraction (noni-ppt; polysaccharide; 0.8 mg in 0.1 ml of juice) while the ethanol-soluble fraction (5.2 mg solid in 0.1 ml of juice; many low-molecular substances including alkaloid, polyphenol, vitamins or other anti-oxidants) showed no antitumor activity.

Antitumor activity of Hawaiian noni-polysaccharide (noni-ppt) on S180 ascites tumor in mice

Methods

The same as above. The allogeneic tumor can grow in any strains of mide (DBA/2, C57BL/6 & BALB/c used). The daily increase in body weight which is paralleled the growth of the ascites tumor was calculated.

Results

The therapeutic treatment with noni-ppt (0.5 mg/mouse, starting day 1, 4-5 X injections) inhibited the tumor growth (T/C = 52%) and produced some cured mice (31%).

Peritoneal exudates cell (PED)-mediated cytotoxicity assay

PEC were elicited by i.p. injections of noni-ppt (0.5 mg/mouse, daily 5 times), then harvested PEC by peritoneal washing, and were coincubated with LLC cells for 48 h in vitro culture plant. It was found that PEC killed 37% of the cancer cells; ca. 9 times stronger kill-activity than that of controls (PBS-elicited PEC). It means that PEC are really activated and are ready to kill the cancer cells by the administration of noni-ppt.

Nitrogen oxide (NO) and cytokine production from the adherent PEC (macrophages) by noni-ppt in cultures

Peritoneal macrophages harvested from normal mice were cultured in the presence of noni-ppt (1.25 mg/ml) for one day. It was found that peritoneal macrophages produced NO and several cytokines including interleukin-l (IL-1), tumor necrosis factor (TNF) and IL-12 in the presence of noni-ppt. IL-12 could stimulate the immune system toward Th1-dominant cellular immunity side.

Cytokine production from splenic or thymic lymphocytes by noni-ppt in cultures

The lymphocytes were cultured in the presence of Con-A (a mitogen, 6 ug/ml) and noni-ppt (1.25 mg/ml). It was found that IL-4 production was decreased; instead interferon-gamma (IFN-r) production was significantly increased. It means that immune system was shifted to Th1-dominant cellular immunity side. The IFN-r stimulated macrophages, NK cells and cytotoxic T cells toward killing tumor cells.

Abrogation of the antitumor potential of noni-ppt with concomitant treatment of immune cell inhibitors in mice

The therapeutic activity of noni-ppt was completely abolished by the concomitant administration of either one of the specific inhibitors of macrophages (2-chloroadenosine: 0.1 mg/mouse, 4 times injections) or T cells (cyclosporine: 2 mg/mouse, day 1). It means that these immune cells must be concertedly functioning to elicit the antitumor potential of noni-ppt.

Effect of chemo-immunotherapy of noni-ppt with standard cytotoxic drugs against LLC in mice

Noni-ppt showed synergistic or additive beneficial effects when combined with several chemotherapeutic drugs such as adriamycin, cisplatin, 5-fluorouracil, and vincristine.