Study of the Operation BIM Mangosteen Juice on the Modulation of the Immune System

During the last decades, development of specific agents affecting T helper cell subpopulations, i.e., Th1, Th2 and Th17, differentiation has drawn special attention. Many natural products were reported as a good agent for modulating the immune response by regulating of the differentiation of T helper cell subpopulations. These products are potential to be the immunemodulators for treatment of various diseases including infectious diseases, cancers, allergy and also autoimmune diseases.

In this study, we aim to study the immunomodulatory effects of the Operation BIM product. We investigate the possible effect of an Operation BIM product, BIM mangosteen juice, on the controlling of T helper cell subpopulation differentiation.

Objectives .

The objective of this study is to investigate the possible effects of the Operation BIM product BIM mangosteen juice on regulation of T helper cell subpopulations. The levels of various cytokines of blood collected from healthy donors before and after taking Operation BIM product (BIM mangosteen juice) for 15 days were compared.

Study approaches:

1. Study subjects

- 12 healthy volunteers: 6 males and 6 females
- Age: 20-55 years old
- The recruited volunteers were separated into 2 groups:
  - Group 1: taking placebo; 6 subjects
  - Group 2: taking BIM mangosteen juice; 6 subjects

2. Blood collections

Blood (5 ml. using heparin as anti-coagulant) were collected from each subject at day 0. According to their groups, subjects took BIM mangosteen juice or placebo (300 ml/day) everyday for 15 days. Afterwards, blood was collected (5 ml. using heparin as anti-coagulant) for the second time at day 16.

3. Study of the effect of the BIM mangosteen juice on the regulation of T helper cell subpopulations

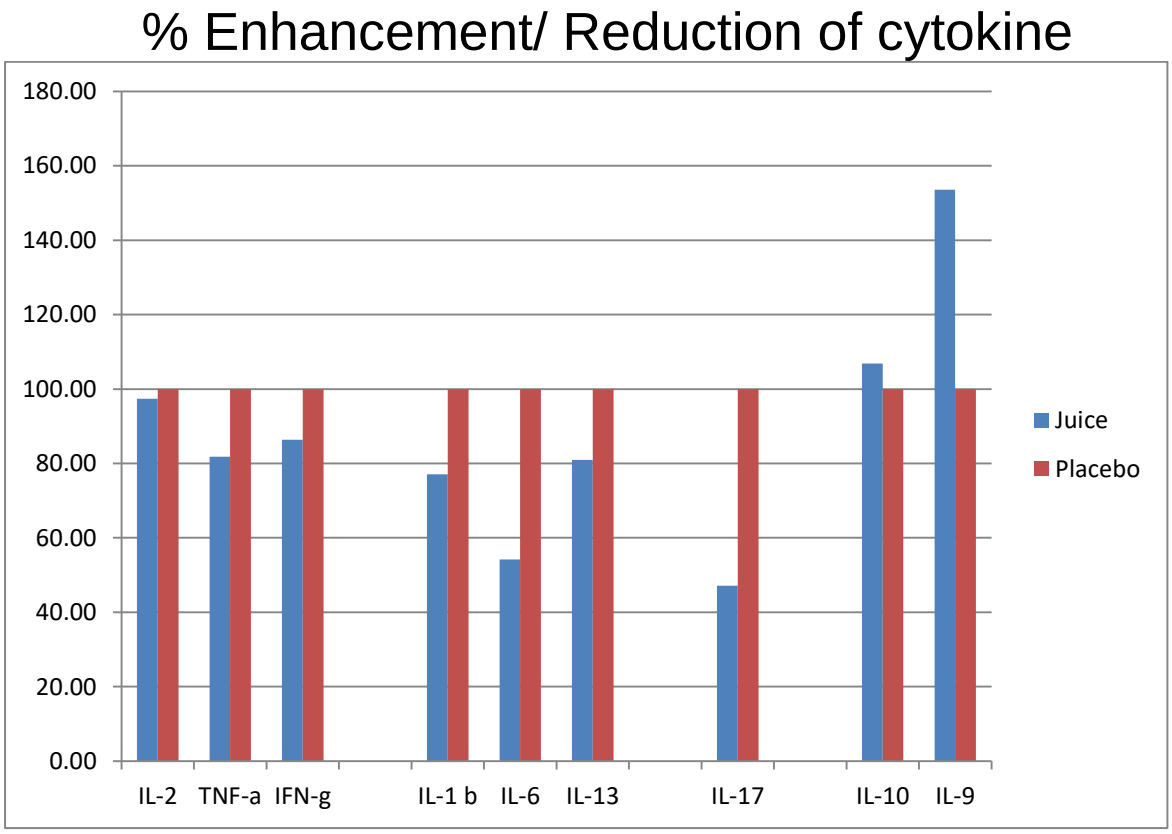
Peripheral blood mononuclear cells (PBMCs) were isolated from the collected blood by using Ficoll-Hypaque gradient centrifugation. PBMCs were *in vitro* stimulated with or without anti-CD3 monoclonal antibodies (clones OKT3) and cultured for 24 hours at 37^{o}C in a CO_2 incubator. The cell cultured supernatant were collected and centrifuged 20,000 rpm, 2 min. The cell free supernatants were separated and stored at -70°C for determination of cytokines.

4. **Determination of T helper cell cytokines**

Cytokines in the cell cultured supernatant were determined by Flow cytomix® (eBioscience, Inc. San Diego, CA, USA) followed the manufacturer's protocol. Comparison of the cytokine levels from un-stimulated PBMC and stimulated PBMC in term of Stimulation Index on day 0 and day 15 were performed.

Results

The stimulation indexes of various cytokines in subjects taking the BIM Mangosteen juice and placebo were calculated and compared. By normalization using subjects taking placebo, % enhancement and reduction of subjects taking BIM Mangosteen juice were shown in Figure below.



The results indicate that BIM mangosteen juice increased the production of IL-9, a proinflammatory cytokine. IL-9 was historically believed to be involved in type 2 immune responses, however, recent evidence suggests IL-9 is secreted by a T helper sub-population named Th9 cell. IL-9 binds to a heterodimeric receptor composed of the γ chain portion (CD132) of the IL-2 receptor and the IL-9R chain. Once bound, it activates the JAK/STAT signaling pathways. Its pleiotropic effects on Th2 lymphocytes, B lymphocytes, mast cells, eosinophils, IgE production has been report. Recently, Th9 cells promote antitumor immune responses *in vivo* have been demonstrated. Th9 cells involve in provoking CD8 CTL-mediated antitumor immunity and Th9 cell-based cancer immunotherapy may be a promising therapeutic approach.

Report by
Professor Dr. Watchara Kasinrerk, Ph.D.
Director; Biomedical Technology Research Center,
Faculty of Associated Medical Sciences,
Chiang Mai University,
Chiang Mai 50200, Thailand