Natramune™ (PDS-2865)® Supplementation Trials: Advancing and Strengthening the Human Immune System.

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Background

The human immune system is an important communication network of cells and tissues which protect the body against infection, tissue damage and diseases including cancer. Recent advances made in measuring and the various component cells and communication channels of the immune system has allowed scientists to test the effects of drugs, natural compounds and nutrients on the various and many features of the immune response. The ability to formulate treatments that improve immune system function is very important since age, physiological demands and natural environmental changes are all known to disrupt the communication network of the immune system and lead to disease. In specific, as humans age, the thymus, which produces T-lymphocytes, undergoes atrophy and the population of T-lymphocytes decreases. In addition to age, stress and poor nutrition decrease both immune system levels and function and it is speculated that this accounts for decreased reproductive health, increased infection, more skin lesions, and cancer.

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Here, we present **Natramune™ (PDS-2865®)**, a nutritional supplement which demonstrates the ability to boost immune system cell numbers and strengthen the immune system communication network and function. **Natramune™ (PDS-2865®)** is a natural obtained hemicellulose (high molecular weight polysaccharide complex) and fatty acid mixture in their naturally occurring ratios, which has been extracted from natural sources available from Gramineae, Poaceae, Dioscoreaceae family of plants and several species of mushrooms using a protected proprietary process. Hemicelluloses are plant and fungal cell wall polysaccharides which are available to human metabolic enzymes. Various hemicellulose preparations have been shown to have a positive impact on the function of cells of the immune system. Consequently there is a great deal of interest in the nutraceutical and health industries to find hemicellulose supplements with proven benefits. Data is presented here which demonstrate the hemicellulose formulation, **Natramune™ (PDS-2865®)** increases immune system cell numbers as well as boosting natural killer cell activity and enhancing other functional aspects of the immune system (1 – 8). Applications for **Natramune™ (PDS-2865®)** include dietary supplements and functional foods, among others.

In previous studies dietary supplementation with **Natramune™ (PDS-2865®)** has been shown to increase immune cell cytokine production (1, 2, 4, 5), stimulate macrophage proliferation (1, 2, 4, 5), increase natural killer cell destruction of cancer cells (1 - 2), provide antioxidant activity (8), reduce inflammation (3) and slow the progressive destruction of the immune system by HIV (1, 2, 6, 7). These studies have already been published in the peer-review scientific literature, are currently under review by editors and experts in the field of immunology or are in the stages of preparation for submission to scientific Journals for review.

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Experimental Designs and General Methods

Clinical Studies: In order to assess the real potential for improved the immune function / activity and health benefits in humans, **Natramune™ (PDS-2865®)** safety, efficacy measures and immunological tests with enumerative measurements and also health-related quality of life were measured in volunteers.

The 18 volunteers (15 healthy and 3 immunosuppressed either with Cancer, HIV or Hepatitis C) enrolled in this open label, single center study had an average age of 45 years (ranging from 18-75 years). They were scheduled for a total of four visits, maintained a regular diet and recorded times of supplementation and meal consumption daily in product use diaries. Volunteers could not be using another immunity boosting product, alternative therapies, or dietary supplements 8 weeks prior to or during the study. Subjects were assigned to take two 250 mg (twice daily) (**Natramune™ (PDS-2865®)** treatment with instructions to consume the coded supplement capsules two in the morning and two in the evening daily for 8 weeks. Weight, medical history, brief physical, blood pressure, patient symptom checklist, CBC, platelets, basic metabolic panel, and flow WBC, NK cells, T-lymphocytes, T helper/inducer, T cytotox/suppressor, B lymphocytes, natural killer cell cytotoxicity, creatinine, and blood glucose were measured at baseline and then at 4 and 8 weeks. All diaries, study capsules, capsules container were collected at each clinic visit. Compliance with treatment supplement regiment was determined by a capsule count and product use diary review.

In Vitro Assays: Macrophages are important cells of the immune system for their ability to engulf and destroy invaders of the host in a process known as phagocytosis. Phagocytosis is also a first important step in the communication network leading to the initiation of the immune response. Therefore the ability of macrophages to phagocytos bacteria was measure in the presence and absence of **Natramune™ (PDS-2865®)**. The furtherance of communication network of the immune system requires signaling molecules such as nitric oxide. Therefore macrophage nitric oxide production was also measured. Lastly, a hyperactivation of the immune system cellular network can result from exposure to chemical pollutants (xenobiotics) and lead to inflammatory damage and disease. Therefore we also measured the ability of **Natramune™ (PDS-2865®)** to restore balance to pesticide treated T-lymphocytes and reduce behavior associated inflammation.

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Results

Clinical Studies: In these studies a cohort of 18 volunteers were supplemented with **Natramune™ (PDS-2865®)** for eight weeks. An analysis of variance (ANOVA) was used to assess the differences between baseline and end of treatment.

(1) significant increases in circulating lymphocyte levels, in healthy subjects and those with impaired immunity ($p = 0.039$)

(2) increases the number of leukocytes, T-cells, B-cells and NK cells (not significant changes)*

(3) significant increases both NK cell activity and NK cell response rate ($p = 0.025$)

*The strict numbers comprising subsets of cells within the immune system network is not necessarily the most important endpoint in the measure of the strength of the immune system. Indeed, increases in cell number were not expected to be significant across the board. The more important parameter is the functional activity of the cells that are available. For example, while natural killer cell populations were not increased significantly in number (#2), on a per cell basis these cells were more active in carrying out function when taken after **Natramune™ (PDS-2865®)** supplementation (#3). This trend to increase immune system function in the absence of an increase immune system cellular population is further reflected by the *in vitro* studies shown below.

However, it is indeed valuable that there was a statistically significant increase in lymphocytes and a general increase in subset cell numbers. This is true especially in the cases of immune suppression and immunodeficiency. For example, the elderly, transplantation patients on immunosuppressive drugs, cancer patient on chemotherapy and HIV infected individuals all face the threat of loss of immune system function through reduced numbers of cell. In this regard, the ability of **Natramune™ (PDS-2865®)** to boost immune system cell numbers offers a far reaching benefit to the maintenance of immune system health.

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In Vitro Studies: Macrophage phagocytosis and nitric oxide production was measured in the presence and absence of **Natramune™ (PDS-2865®)**. Further, T-lymphocytes were forced to exhibit behaviors associated with inflammation and the ability of **Natramune™ (PDS-2865®)** to block this hyperactivation was measured. The statistical comparison of the treatment groups (with and without **Natramune™ (PDS-2865®)**) was determined using a student's t-test.

(1) significant increases phagocytotic activity of macrophages ($p < 0.001$)

(2) significant reduces xenobiotic-induced T-cell inflammatory hyperactivation ($p = 0.009$)

(3) significant increases NO release by macrophages ($p < 0.001$)

Note that **Natramune™ (PDS-2865®)** has significant effects on all of the above measured functions of the immune system activities. In these studies, the same number of cells was used, so again we see increased phagocytosis and nitric oxide (NO) production with **Natramune™ (PDS-2865®)** application. These activities demonstrate the positive value of **Natramune™ (PDS-2865®)** on the immune system function and communication networks. The ability of **Natramune™ (PDS-2865®)** to reduce inflammatory behavior is also indicative of a healthy and balanced immune system.

The comparison and contrast between cell numbers and cell function when measuring the benefits of **Natramune™ (PDS-2865®)** on immune system function is summarized and highlighted in table 1.

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Conclusions

1) **Natramune™ (PDS-2865®)** supplementation significantly increases human lymphocyte levels and stimulates general increases in immune system cell subset levels. This results shows that **Natramune™ (PDS-2865®)** is an excellent supplement to fight immunosuppression (elderly, cancer patients , transplantation patients) and immunodeficiency (genetic diseases, nutritional deficiencies and HIV/AIDS)

2) **Natramune™ (PDS-2865®)** supplementation increases human natural killer cell responsiveness and cytotoxicity. Natural killer cells are known in particular to rid the body of cancer cells. Therefore, **Natramune™ (PDS-2865®)** is a valuable supplement in the nutritional fight against cancer.

3) **Natramune™ (PDS-2865®)** increases immune system cell functions, not just numbers or circulating levels. Therefore, a person with peak immune system cell numbers can still benefit from **Natramune™ (PDS-2865®)** supplementation through enhance phagocytosis, nitric oxide production cellular communication and protection from inflammatory damage.

The data presented here include the most recent results in a series of peer-reviewed publications that add to the body of literature from Innovation Laboratories which prove that hemicellulose supplementation in the form of **Natramune™ (PDS-2865®)** boosts immune system function and is a valuable component of the nutraceutical industry.

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Table 1. The benefits of Natramune™ (PDS-2865®) on immune system cell numbers and function.

	Effect of Natramune Supplementation (% change)
Circulating Cell Numbers	
Leukocytes	**+14.5**
Total Lymphocytes	**+18.0***
B-lymphocytes	**+10.1**
T-Lymphocytes	**+6.8**
Cytotoxic T-Lymphocytes	**+18.3**
Helper T-Lymphocytes	**+10.0**
Natural Killer Cells	**+14.4**
Cellular Function	
Killer Cell Response rate	**+15.0***
Killer Cell cytotoxicity	**+26.0***
Phagocytosis	**+65.0***
Inflammation	**-80.0***
Nitric Oxide Production	**+517.0***

***Statistically significant changes when compared to pre-supplementation values.**

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References

1. *Schavoustie* SE, Perez PP, Flecther MA, Maher KJ, Mitrani AA, Thomas RH: Clinical study on Natramune (PDS-2865) at the Clinical Immunology-University of Miami School of Medicine, 2002.

2. *Schavoustie* SE, Perez PP, Flecther MA, Maher KJ, Mitrani AA, Thomas RH: Pilot Study: Effect of PDS-2865 on natural killer cell cytotoxicty. JANA, 2003; 6(2): 39-42

3. *Weeks BS, Lee SW, Perez PP, Brown K, Chauhan H, Tsaava T: Natramune and PureWay-C reduce xenobiotic-induced human T-cell $\alpha 5\beta 1$ integrin-mediated adhesion to fibronectin.* [PubMed - in process]

4. *Rodriguez MM, Mejia JC, Blanchard MT, Stott J, Pestano N, Perez PP: Pilot Study: The Effects of Natramune (PDS-2865), A new immunostimulator supplement on different Cetacean Species; Tursiops truncatus, Lagenorhynchus obliquidens, and Orcinus orca.* [PubMed - in process]

5. *Rodriguez MM, Mejia JC, Blanchard MT, Stott J, Pestano N, Perez PP: Oral administration of Natramune (PDS-2865) to animals of the Cetacean Species: Effects on the Immune System.* [PubMed - in process]

6. *Macrophage activating property of the Natramune (PDS-2865) in a macrophage phagocytosis assay using J774A.1 murine macrophages.* [PubMed - in process]

7. *Nitric oxide releasing activity of the Natramune (PDS-2865).* [PubMed - in process]

8. *ORAC and DPPH free radical scavenging values of Natramune (PDS-2865).* [PubMed - in process]

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