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Comparison

Nowadays, foods with health benefits have become very popular. Functional foods are regularly introduced into our diet. More and more manufacturers are jumping on the healthy food bandwagon, but not all extracts are created equal and their products differ widely in composition and, subsequently, in quality and activity. With very few comparative studies available, the consumer needs to do homework. Natural immunomodulators offering strong activity and no side effects have been sought for centuries. The current market is full of both individual immunomodulators and various combinations all promising the golden fleece-inexpensive and active stimulation of immune reactions.

Inexpensive and effective natural immunomodulators represent a holy grail of current alternative medicine. Some have been extensively studied for decades with an impressive number of peer-reviewed scientific papers (such as glucan), while some give confusing results based on isolation sources (such as *Echinacea*, where results widely differ based on the part of plant used for isolation) (Barret et al., 1999). When we consider some differences between individual batches, based on the natural source of material, it is understandable why big pharmaceutical companies still are not convinced. Some of the natural immunomodulators have already reached clinical trials and with dozens of clinical trials under way, their use in regular clinical practice is only a question of time. However, despite clear and well-established biological effects of this immunomodulator, the search for even better effects continues.

To date, very few papers have compared individual immunostimulators (Wilasrusmee et al., 2002, Saldanha and Tollefsbol, 2012). Based on the limited published comparisons, we decided to compare numerous commercially available immunostimulators. To do this, we used every immunomodulator

mentioned in this book––*Astragalus*, ellagic acid, *Chlorella*, cat's claw, Glucan #300, ginseng, elderberry, thyme essential oil, and *Echinacea*––with only one aim, to test them against each other in well-established reactions. Discovering small natural molecules that regulate the immune system will increase our understanding of how diet and nutrition improve immune functions. The objective of this study was to compare individual natural molecules with demonstrated immunostimulating properties.

Stimulation of phagocytosis is usually the first effect of any natural immunomodulator. Using a model of synthetic polymeric 2-hydroxyethylmethacrylate microspheres, we measured the phagocytic activity after feeding with tested substances for two weeks. Our data are summarized in Figure 19 and show that only glucan and *Astragalus* significantly increased phagocytic activity of blood neutrophils and peritoneal macrophages

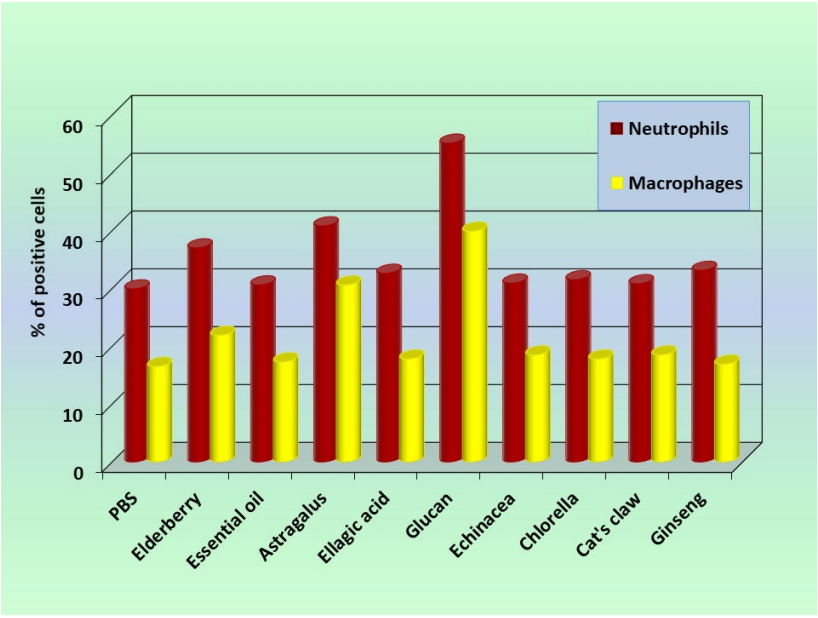

Figure 19 Effects on phagocytosis

The next part of our study focused on production of IL-2. IL-2 levels were measured after a 72-hr. *in vitro* incubation of spleen cells isolated from control and stimulant-treated animals. Since the secretion of IL-2 by nonstimulated cells (PBS) was always a zero, all

tested material showed significant stimulation of IL-2 production (Figure 20). The most active materials were elderberry, *Astragalus*, ellagic acid, and glucan. Essential oil had no effects at all.

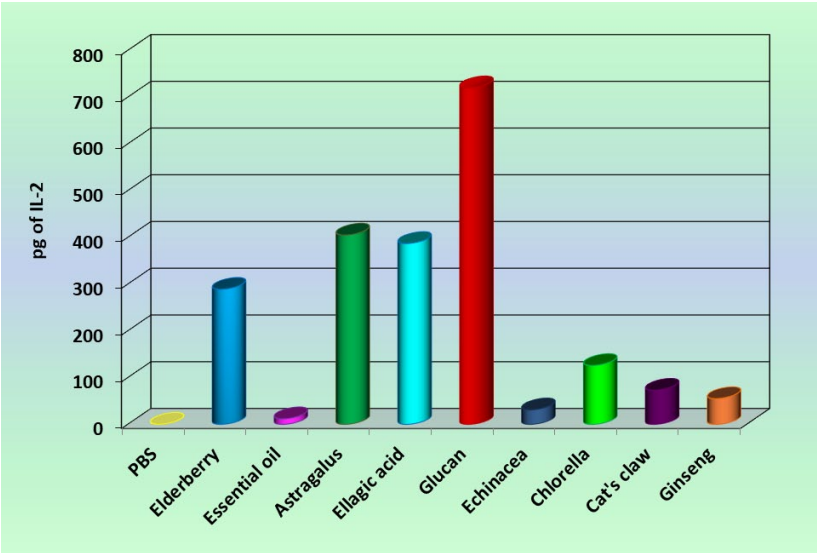

Figure 20 Effects on production of IL-2

Most natural immunomodulators stimulate cellular immunity; however, recent studies also showed significant effects on humoral branch. As an experimental model, we used immunization with ovalbumin as an antigen. Mice were injected twice with albumin and the serum was collected 7 days after the final injection. All tested samples stimulated antibody formation to some extent, with the glucan stimulation being by far the strongest (Figure 21).

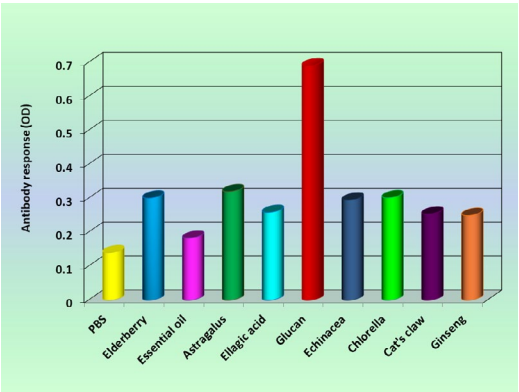

Figure 21
Effects on antibody formation

We then focused on the role of tested substances in cancer inhibition. Using a model of Lewis lung carcinoma cells, we showed that cyclophosphamide caused 70% inhibition of the number of lung metastases in comparison to the control group (Vetvicka et al., 2007). However, cyclophosphamide is a strong chemotherapeutic drug and we tried to find out if we can use a natural modulator instead. Our data summarized in Figure 22 show that only glucan significantly lowered the number of lung metastases. Whereas any of the tested materials showed only few percent inhibition (if any inhibition at all), glucan showing 47% inhibition

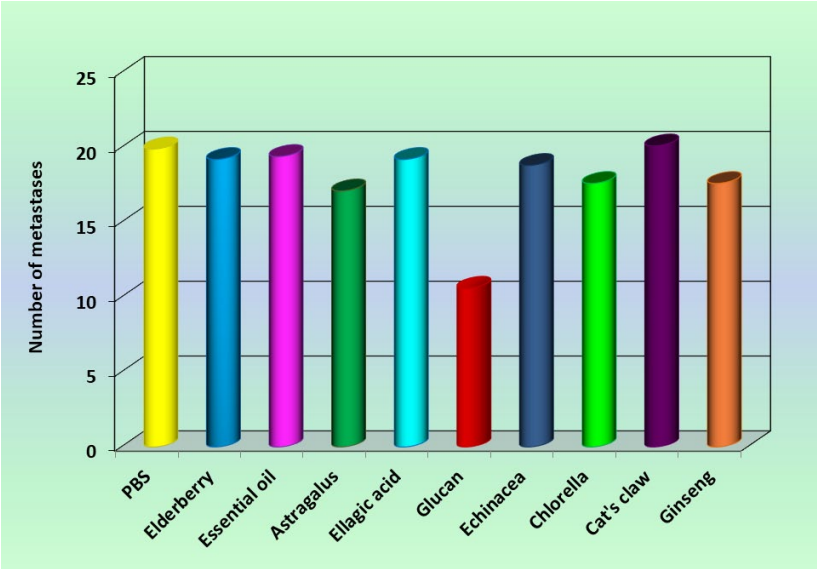

Figure 22 Effects on inhibition of lung cancer

Our last experiments focused on NK cell activity, which is an important immunological feature involved in numerous defense mechanisms, particularly in detection and elimination of viruses and cancer (Cerwenka and Lanier, 2016). Our experiments showed that some samples (e.g., essential oil) had no activity and others demonstrated mediocre activity (Figure 23).

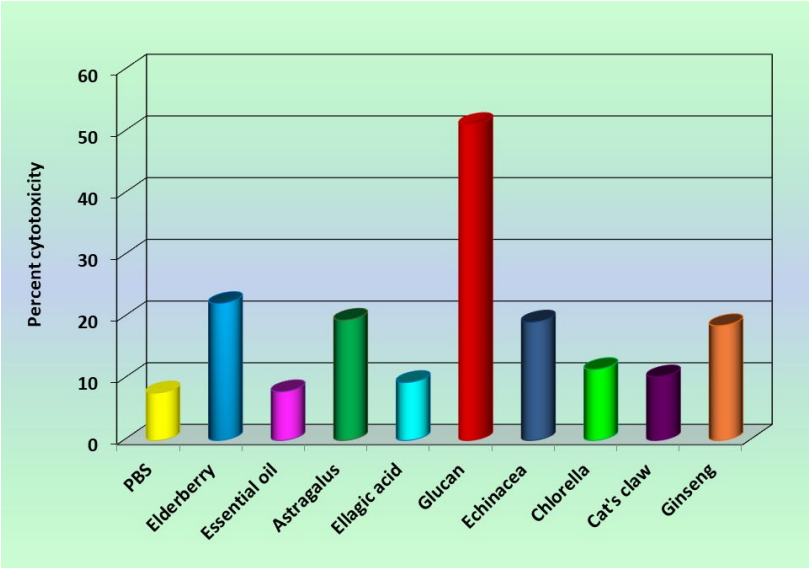

Figure 23 Effects on NK cell activity

The only supplement with high potential to activate NK cells was glucan #300, which was already established both in animal (Vetvicka and Vetvickova, 2015) and human (Pohorska et al., 2016) models.

Several conclusions can be made—most of the commercial immunostimulating compounds have only very limited, if any, effects on the immune system including cancer. In addition, doses recommended on the label might not be sufficient, but no solid data on dosages exist with the exception of glucan (Vetvicka and Vetvickova, 2010). Experiments summarized in this Chapter clearly demonstrated that among all tested supplements, only glucan offered consistent immunoenhancing activities. Similar data were previously published (Vetvicka and Vetvickova, 2014). As glucan emerged as a clear winner, it is not surprising that direct comparisons of individual supplements do not exist, as most samples would be shown to have little or no activity. In this regards, individual commercial glucans were repeatedly tested against each other (Vetvicka and Vetvickova, 2005, 2007, 2010, 2014).

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