

Mobilization of bone marrow stem cells with StemEnhance® improves muscle regeneration in cardiotoxin-induced muscle injury

Introduction

It was shown that stem cells released from the bone marrow can migrate into injured tissues, supporting the process of tissue repair. In this process, the number of circulating stem cells was shown to be a critical factor. In a number of studies addressing various health conditions, higher numbers of circulating stem cells have been associated with greater health. An increase in the number of circulating stem cells was shown to improve various health conditions.

Based on this information, it was claimed that the natural stem cell mobilizer StemEnhance had the ability to support optimal health by increasing the number of circulating stem cells. StemEnhance is an extract from the aquatic botanical *Aphanizomenon flos-aquae* that was shown in a double-blind crossover study to increase the number of circulating stem cells by 25-30%.

This study was aimed at confirming the effect of StemEnhance™ on tissue repair.

Methods

In brief, thirty 8-10 weeks old female mice were lethally irradiated before receiving a bone marrow transplant with stem cells marked with green-fluorescent protein (GFP). After transplantation, animals were randomly separated into two groups of 15 animals, one group received placebo while the other received 300mg/kg/day. At day 16 and 30

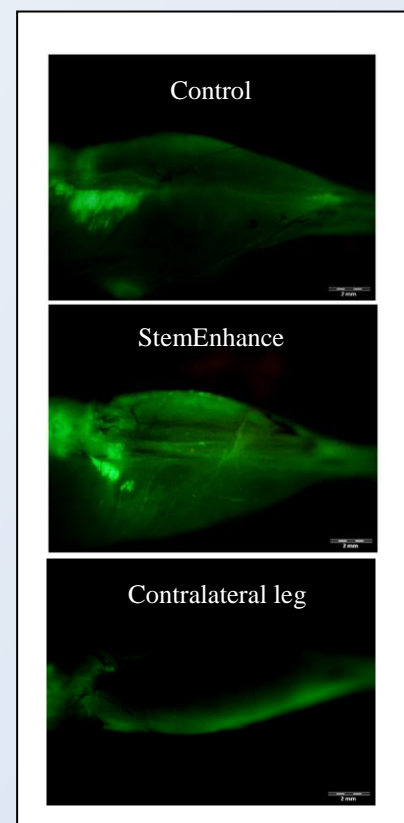
after transplantation, mice from each group were randomly selected for hematological tests to see the effect of StemEnhance on hematopoiesis. The remaining mice in each group (n=6) were injured by injection of 10µm Cardiotoxin in 100 µl PBS directly into the anterior tibia muscles of right leg. Five weeks after the injury, the mice were sacrificed and using open imaging (Olympus OV 100 Small Animal Imaging System), the mice were evaluated for incorporation of GFP cells into tissues, including heart muscle, liver, kidneys, intestinal wall, brain, skin and lung. The incorporation of GFP-positive muscle fibers was quantified with Photoshop 7.0.

Results

No significant difference was observed between the treated (StemEnhance) group and untreated (PBS) group regarding average hemoglobin content as well as WBC, RBC platelet and reticulocytes counts. Therefore StemEnhance did not appear to have an effect on hematopoietic recovery.

In the injury part of the study, the extent of the recovery was evaluated by measuring the area covered by fluorescence in the recovering muscles. The group receiving StemEnhance showed greater regeneration of the tibialis muscle ($p<0.05$), though both PBS and StemEnhance groups showed very significant recovery. The difference between the two groups was also noted behaviorally by a greater strength in the leg of the StemEnhance group while being handled, though this was not quantified.

Less fluorescence was seen in the contralateral left tibialis muscle of both groups, indicating that migration of bone marrow stem cells was more significantly directed toward the injury.



Some fluorescence was also seen in most of the main organs, such as the heart, brain, kidney, liver and lung, though no difference was seen between the two groups.

Discussion

StemEnhance did not seem to have an effect on hematopoietic recovery, as it did not increase the number of red blood cells, white blood cells and platelets soon after irradiation. However, StemEnhance did enhance recovery from cardiotoxin-induced muscle injury. Reliable measurements of fluorescence were not made during the healing process, therefore it is not possible to discriminate whether StemEnhance accelerated the repair process or enhanced the overall repair process. Studies have reported that bone marrow stem cell mobilization accelerates the healing of skin burn and bone fracture. On the other hand, it was reported that scar formation appears to take place when not enough stem cells are available to support full repair process. So it is likely that the effect of StemEnhance was an acceleration of the repair process, which in some conditions could also lead to a greater overall repair by reducing scar formation.

While StemEnhance enhanced recovery, significant recovery was nonetheless seen in the control group indicating stem cells derived from the bone marrow naturally contribute to the repair of injuries. Furthermore, in both StemEnhance and control group, incorporation of GFP-muscle cell was much less in the contralateral left tibialis muscle, indicating that stem cells migrate predominantly towards sites of injury. Therefore, this study confirms three key aspects of stem cell physiology: 1) stem cell migration in an injured tissue is a natural process that takes place without any stimulation, 2) increasing the number of circulating stem cells accelerates the repair process, and 3) stem cells primarily migrate to sites of injuries.

In conclusion, this study confirmed the hypothesis that StemEnhance supports the natural process of tissue repair by supporting the release of stem cells from the bone marrow.