



Natural Immune Systems Inc

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Report for:

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Report 14: Evaluation of the effects of Jobelyn™ consumption on red blood cell count and quality.

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Report 14. Evaluation of the effects of Jobelyn™ consumption on red blood cell count and quality.

Executive Summary

The goals for this clinical study were to examine the effects of Jobelyn™ on the blood count in general, and specifically on red blood cell health in a borderline anemic, otherwise healthy North American population, as a parallel to several studies performed in West Africa, where sickle cell anemia, HIV, malaria, and other microbial diseases affecting red blood cell health, production, and senescence, are prevalent.

The outcomes were clear, and included the following:

1) Safety documentation

Overall, people consuming Jobelyn™ for 8 weeks had a similar blood count profile as people consuming placebo for 8 weeks.

2) Red blood cell health

People consuming Jobelyn™ showed extremely small, but significant changes to red blood cell parameters. However, the changes were not as simple as expected, and point to a complex array of effects in bone marrow and spleen with consumption of Jobelyn™. The surprising reduction in red blood cell counts (mild, but significant), accompanied by an increase in mean cell volume, and changes in other parameters reveals a complex effect of Jobelyn™ on formation of blood cells, suggesting an improved clearance of senescent RBC, accompanied by increased production of new RBC. The changes may also be related to a reduced inflammatory status. Further testing of cytokine profile will help put this data into context.

3) Effects on immune cells

Consumption of Jobelyn™ was associated with a rapid increase in the blood levels of monocytes and platelets. Whether this is associated with immune activation as well as bone marrow support is a question for future study.

4) Blood glucose

Consumption of Jobelyn™ was in general not associated with reduced fasting blood glucose in this study population. A few cases showed rapid changes, and based on this data further work may be planned.

During the study serum samples were banked from each blood draw. This material is available to pursue further testing without repeating the clinical part of the study. Serum testing may include detailed analysis of pro- and anti-inflammatory cytokines, as well as stem cell related growth factors.

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Report

Purpose

The purpose of the study was to evaluate the timing and magnitude of improvements to red blood cell health with consumption of Jobelyn™, to incorporate data into existing marketing efforts and to publish data in the medical literature as a peer-reviewed credible publication.

Introduction

Health Forever Products has case studies in Nigeria, as well as testimonials from all over the world, of seeing a robust increase in hemoglobin within days and within a few weeks, in people with serious cases of anemia present under either disease conditions like sickle cell, Malaria, HIV, or cancer. In parallel, improvements in red blood cell health were also seen in many healthy people with general low blood counts due to undetermined factors.

A clinical study on anemia is currently ongoing in Nigeria. The study population is focused on women and aims at evaluating whether Jobelyn™ consumption can help increase hemoglobin and thus reduce risk factors associated with gynecological surgery.

<http://clinicaltrials.gov/ct2/show/NCT01670955>

As a parallel to the ongoing study in Nigeria, this study protocol helped to systematically examine the effects of Jobelyn™ on anemic conditions in an otherwise healthy population, and helped document the speed and magnitude of improvements in a population without concomitant infections or sickle cell anemia.

Study design

Twenty-five human subjects of both genders were enrolled, and twenty-three completed the study with testing over the period of 8 weeks. Both genders were enrolled in the study, but we expected more women to be eligible, due to effects of menses and prolonged consumption of birth control pills.

Recruiting of study participants happened via NIS Labs. The study location was Klamath Falls, Oregon, which is located in the high desert of central Oregon, where people live and work at an altitude of 4,000-5,000 feet above sea level.

Subjects were monitored at baseline, and after 3 days, 7 days, and 2, 4, and 8 weeks.

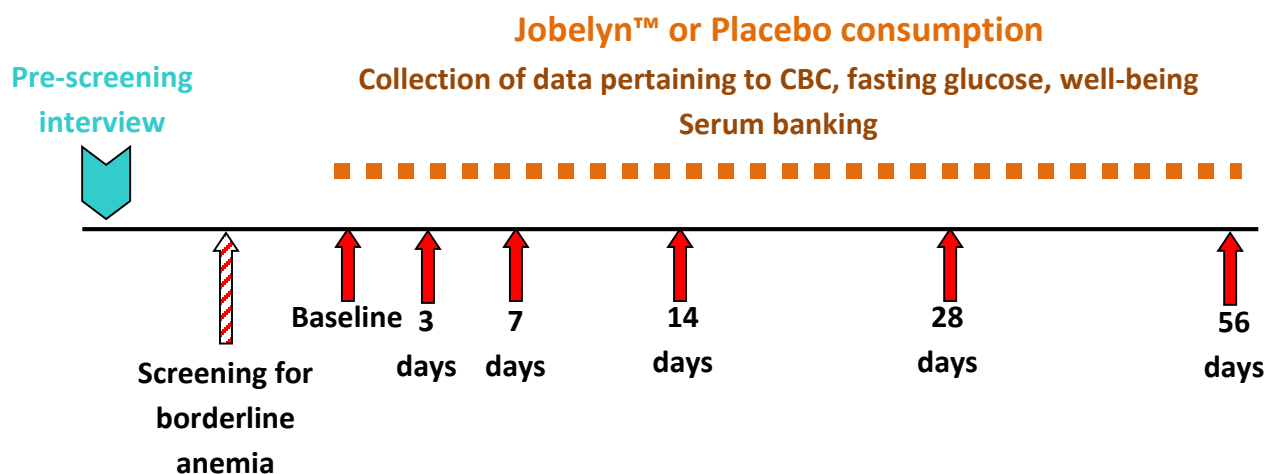


Figure 1. Diagram illustrating the involvement of each human subject.

A blood sample was taken at each visit. The primary purpose of the blood draws was to perform a complete blood count (CBC) with differential count. Each CBC was performed in triplicate at NIS Labs, using an AC-T 5-diff Coulter counter (Beckman-Coulter).

Fasting blood glucose was performed using a glucometer which was calibrated on each morning of every clinic visit for this study.

The blood draws also allowed for serum banking. This provides the option to add testing later without having to repeat a clinical study. Such testing may include antioxidant status and a number of test types for collecting data on inflammatory status. The baseline, 7 day, and 4, and 8 week samples align with the planned blood draws from the proposed chronic pain study, and this will allow synchronized testing at a later time, and a combined evaluation of inflammatory and other metabolic markers across both studies. This will allow data collection of antioxidant capacity and anti-inflammatory effects of Jobelyn™ across several studies, for a more robust sample size.

Study population

We recruited a total of 25 healthy subjects of both genders. Upon written informed consent, they went through a screening process to verify anemia or borderline anemic conditions. They were randomized to receive either Jobelyn™ or placebo.

Inclusion criteria

- 18-65 year old people of both genders
- Borderline anemic (This is compensated for 4,000-5,00 feet altitude of study location):
 - Males: Hemoglobin 13.5 g/dL or lower
 - Females: Hemoglobin 11.5 g/dL or lower

Exclusion criteria

- Known diagnosis with pernicious, aplastic, or sickle cell anemia, thalassemias;
- Splenectomy;
- Serious active illness within past 12 months;
- Active cancer and/or chemotherapy within the last 12 months;
- Major surgery during past 8 weeks;
- Received blood transfusion past 8 weeks;
- Having donated blood for 6 weeks prior to study, or planning to donate blood during the 8 week study;
- Consuming high doses of vitamin B12;
- Significant active uncontrolled disease (such as lymphoma, cirrhosis, nephritis, uncompensated heart failure);
- Use of multiple medications, indicating that the person's self-reported state of 'good health' is questionable;
- History of drug abuse past 2 years;
- Record of non-compliance in previous studies;
- Display of cognitive impairment or mental instability during pre-screening and screening;
- Poor compliance during screening visits;
- Any other condition or observation that the study coordinator judges may adversely affect the person's ability to complete the study;
- Currently experiencing intense stressful events/ life changes that would negatively affect compliance;
- Pregnant, nursing, or trying to become pregnant;
- Women not using effective contraception;
- Food allergies related to ingredients in test product.

Prescreening

The pre-screening involved an interview to document gender, age, estimated BMI, medical/surgical history, diet/lifestyle, current health issues, medication, and supplement use.

Screening

The screening visit involved signing a consent form, asking specific questions, verifying current BMI, and taking a blood draw to determine baseline hemoglobin levels.

Demographics of the study population

We recruited a total of 25 healthy subjects of both genders. Upon written informed consent, they went through a screening process to verify anemia or borderline anemic conditions. They were randomized to receive either Jobelyn™ or placebo.

Table 1. Demographics of study participants.

	Jobelyn™	Placebo
Females:	7	8
Age average*	44.1 ± 16.2	55.6 ± 7.5
Age range	20.9 - 65.3	44.4 - 64.6
BMI average*	26.3 ± 4.3	25.5 ± 5.7
BMI range	22.7 - 34.4	18.2 - 32.9
Males:	5	5
Age average*	56.7 ± 5.9	40.2 ± 18.8
Age range	49.4 - 63	22.3 - 64.1
BMI average*	31.3 ± 4.9	27 ± 4.6
BMI range	26 - 38.8	20.5 - 31.1

* The average ± standard deviation is shown.

Consumables

Jobelyn™ was provided by Health Forever Products. A placebo powder was produced by NIS Labs. Rice flour was used, as it represents another grain, and of a type that very few people have allergies to. Other presumed inert substances can cause gastrointestinal upset, or have their own biological effects. Food color was added to the rice flour until a desired color was reached, and then was crushed into a powder that resembled Jobelyn™. The product and placebo were both encapsulated in identical, clear capsules.

Each study participant consumed 2 capsules per day during the study. This translated to the consumption of 500mg of Jobelyn™ for the people in the Jobelyn™ group.

Recruitment

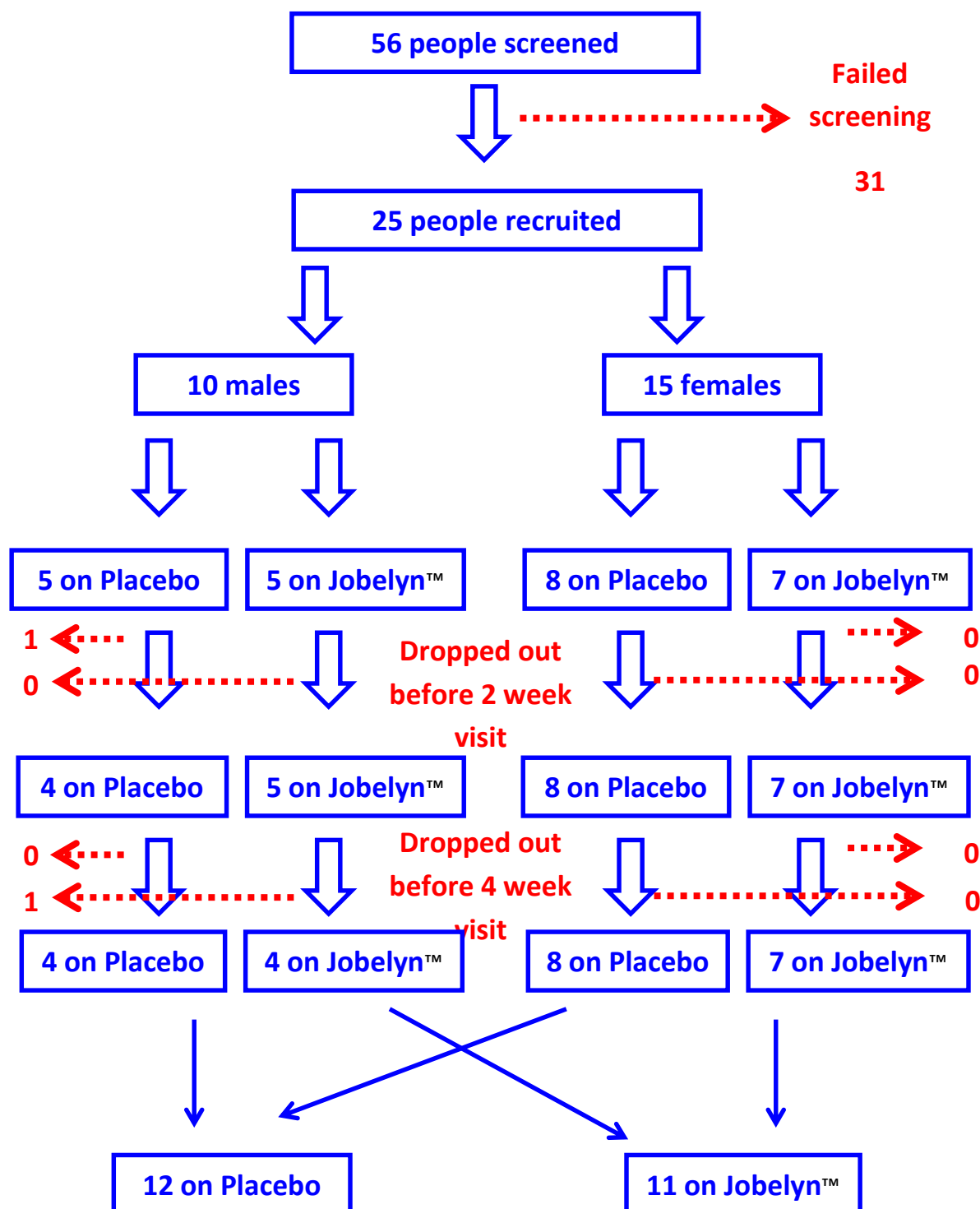


Figure 2. Consort flow chart of the study participants.

Randomization

For a study of this nature, it is ideal to randomize study participants of each gender separately, so there is less risk of having more people of one gender in the placebo group and of the other gender in the active product group. Therefore, the randomization was performed as follows: A coin was tossed to determine the group assignment of the first female study participant. The first male study participant was then allocated to the other group. For subsequent volunteers, the group assignment was assigned alternately within each gender. The exception was family members or very close friends, who would be assigned to the same group to eliminate the risk of an accidental switch of bottles during the study within one household.

Compliance

Compliance during a study involves adhering to the study guidelines and consuming the allocated test product on a daily basis, as well as avoiding making major life style or diet changes during the study.

Compliance pertaining to consumptions was tracked by counting the remaining capsules in the returned bottles. Compliance to other requirements was tracked during interviews at each visit.

Table 2. Compliance based on capsule count.

	Average compliance (%)*
Compliance during first 2 weeks	96.59%
Compliance during second two weeks	94.37%
Compliance during last 4 weeks	96.36%
Compliance during entire study	97.12%

** These % include all study participants, except drop-outs.*

Statistical analysis

Two kinds of statistical analyses were performed. The independent 2-tailed t-test was used to examine differences between the Jobelyn™ and placebo group for each time point. The unpaired t-test was performed both on raw data and on the percent changes seen for each parameter.

In addition, the paired t-test was used to compare each group's scores before and after the intervention. This type of statistical analysis is ideal for comparing repeat measurements of the same subject over time.

Results

The complete blood count (CBC) data is presented in the following order:

- White blood cell count (WBC)
- Red blood cell count (RBC)
- Hemoglobin (HGB)
- Hematocrit (HCT)
- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin (MCH)
- Mean corpuscular hemoglobin concentration (MCHC)
- Red cell distribution width (RDW)
- Platelet (PLT)
- Mean platelet volume (MPV)
- Neutrophil percentages (NE%)
- Lymphocyte percentages (LY%)
- Monocyte percentages (MO%)
- Eosinophil percentages (EO%)
- Basophil percentages (BA%)
- Neutrophil number (NE#)
- Lymphocyte number (LY#)
- Monocyte number (MO#)
- Eosinophil number (EO#)
- Basophil number (BA#)

On the following pages, data graphs are shown for each CBC parameter. For each parameter, there are two graphs, reflecting two different ways of analyzing the data.

- **Top graphs:**
 - Data are shown in a graph format that allows '*between-group*' analysis, using the independent 2-tailed t-test.
 - For most data sets, there are no significant differences at any time point between the two groups.
- **Bottom graphs:**
 - The exact same data are shown in a format that allows a closer look at any minor fluctuations within each group, and allows indication of statistical significant changes within each group, using the '*within-subject*' paired 2-tailed t-test.
 - Many graphs show one of the following:
 - Some significant changes within the Jobelyn™ group, without a matching change in the placebo group.
 - Or no change in Jobelyn™ group, despite a change in the Placebo group, such as may be caused by seasonal changes including allergies.

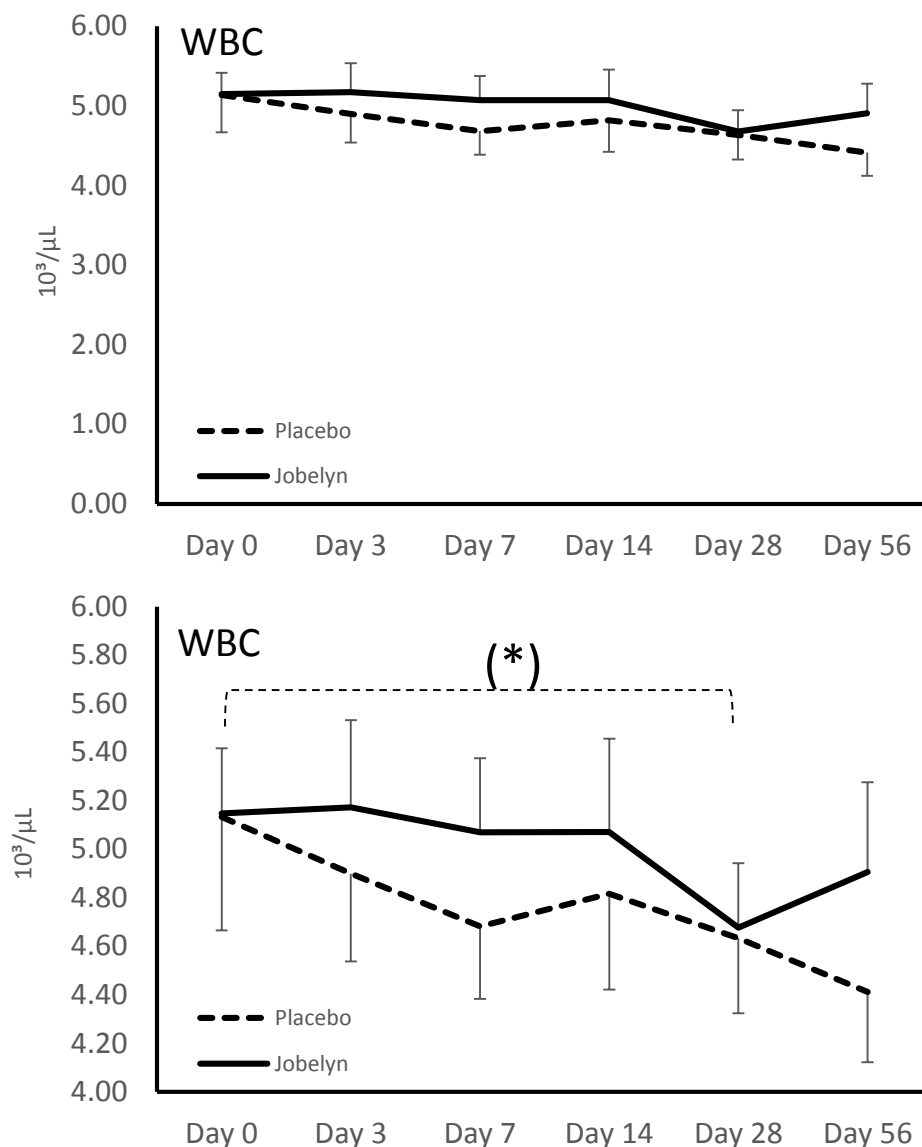


Figure 3. White blood cell (WBC) counts are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average WBC counts in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, minor fluctuations in WBC counts were seen. A general mild reduction in WBC counts were seen for the placebo group over the 8 week study period. During the same time, no change was seen in the group consuming Jobelyn™, except a drop at Day 28 (borderline significant (*) when compared to baseline), which returned to the original level at 8 weeks. ***The data suggest that seasonal or other environmental changes occurring in the general population during that time were not affecting people as much if they were consuming Jobelyn™.***

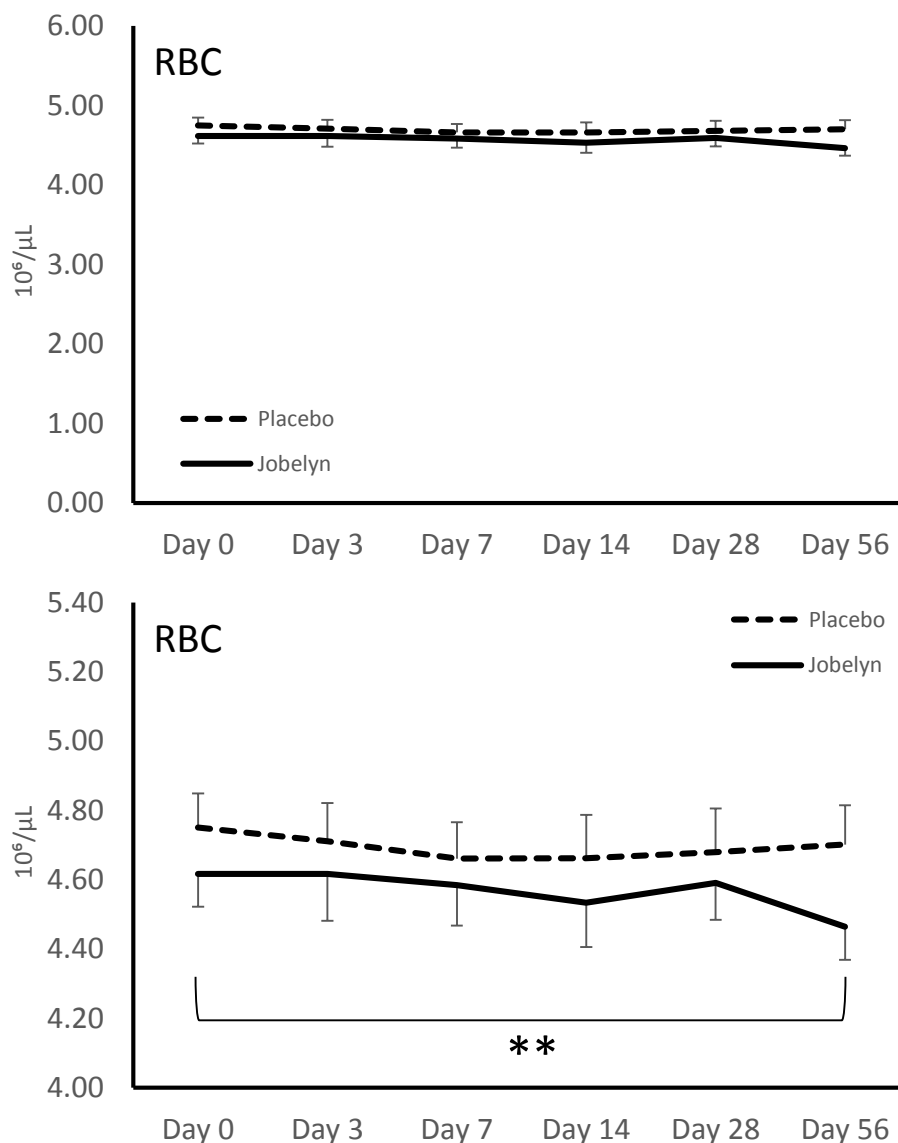


Figure 4. Red blood cell (RBC) counts are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average RBC counts in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, minor fluctuations in RBC counts were seen over time in the Jobelyn™ group ($p < 0.01$, **). During the same time, no change was seen in the group consuming Placebo. ***The data suggest that Jobelyn™’s support of macrophage function may lead to an improved clearance of senescent RBC in the spleen, which if the study had been longer (3-4 months), and had allowed for a complete replenishment of the RBC pool, should be expected to return to normal.***

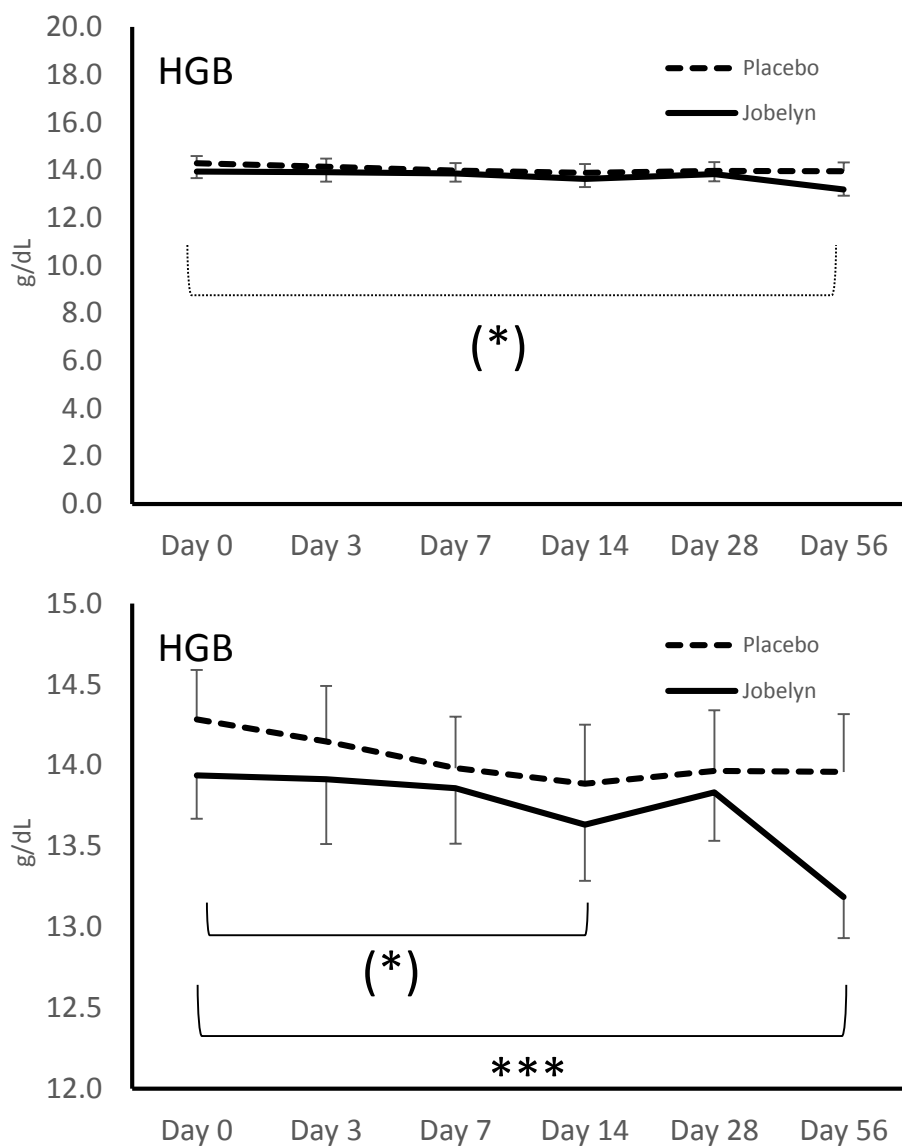


Figure 5. Hemoglobin levels (HGB) (g/dL) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average hemoglobin levels in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when ‘*within-subject*’ analysis was performed for each group separately, minor fluctuations in hemoglobin were seen. A mild reduction in hemoglobin was seen for the group consuming Jobelyn™ at Day 56 ($p < 0.001$, ***) when compared to baseline for the Jobelyn™ group). This follows the data for the red blood cell (RBC) count.

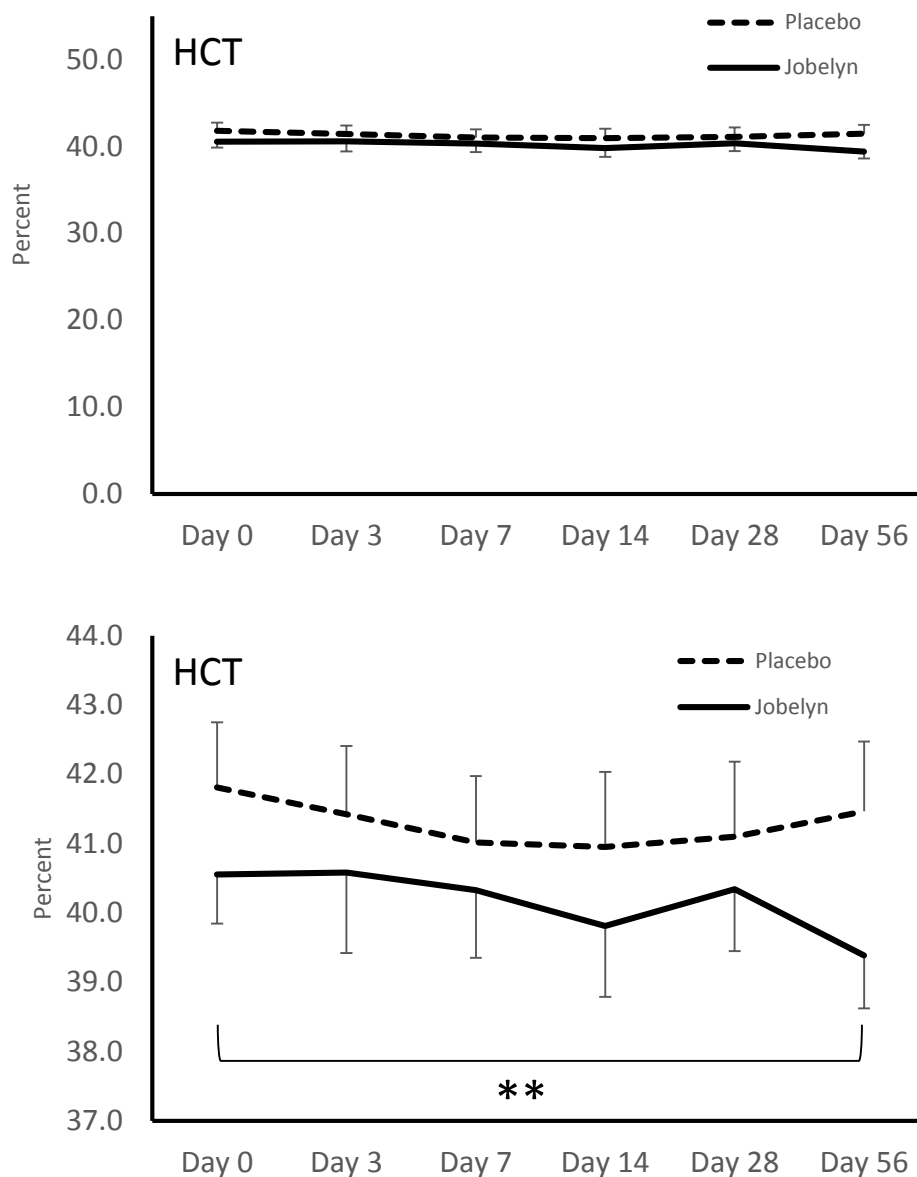


Figure 6. Hematocrit (HCT) (% volume) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average hematocrit in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘*within-subject*’ analysis was performed for each group separately, minor fluctuations in hematocrit were seen. A very mild reduction in hematocrit was seen for the group consuming Jobelyn™ at Day 56 ($p < 0.01$, **) when compared to baseline for the Jobelyn™ group). This follows the data for the red blood cell (RBC) count.

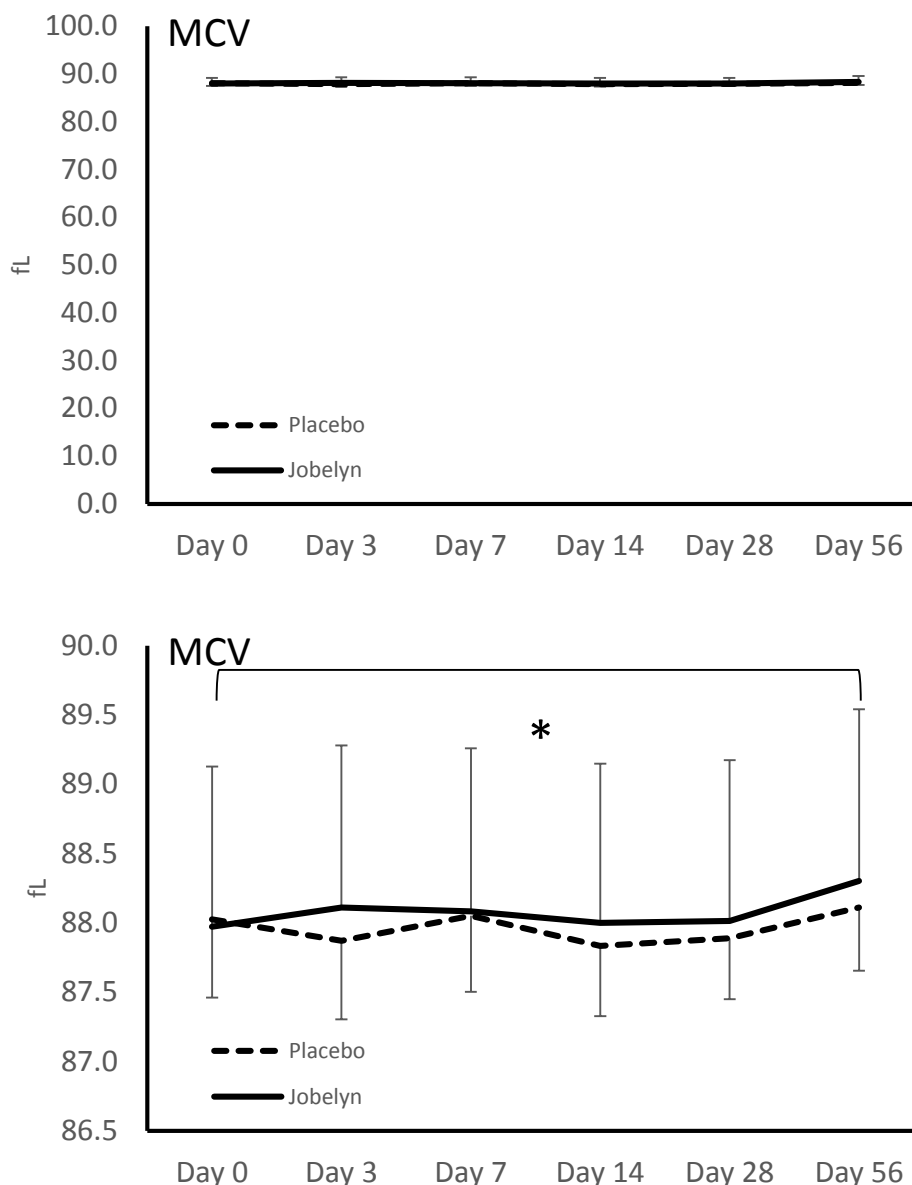


Figure 7. Mean corpuscular volume (MCV) is shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average MCV in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, minor fluctuations in MCV were seen. A very mild increase in MCV was seen for the group consuming Jobelyn™ at Day 56 ($p < 0.05$, *) when compared to baseline for the Jobelyn™ group. ***Interestingly this change seen in the context of the previous red blood cell associated parameters may suggest that over time, with daily consumption of Jobelyn™, fewer but larger red blood cells are produced.***

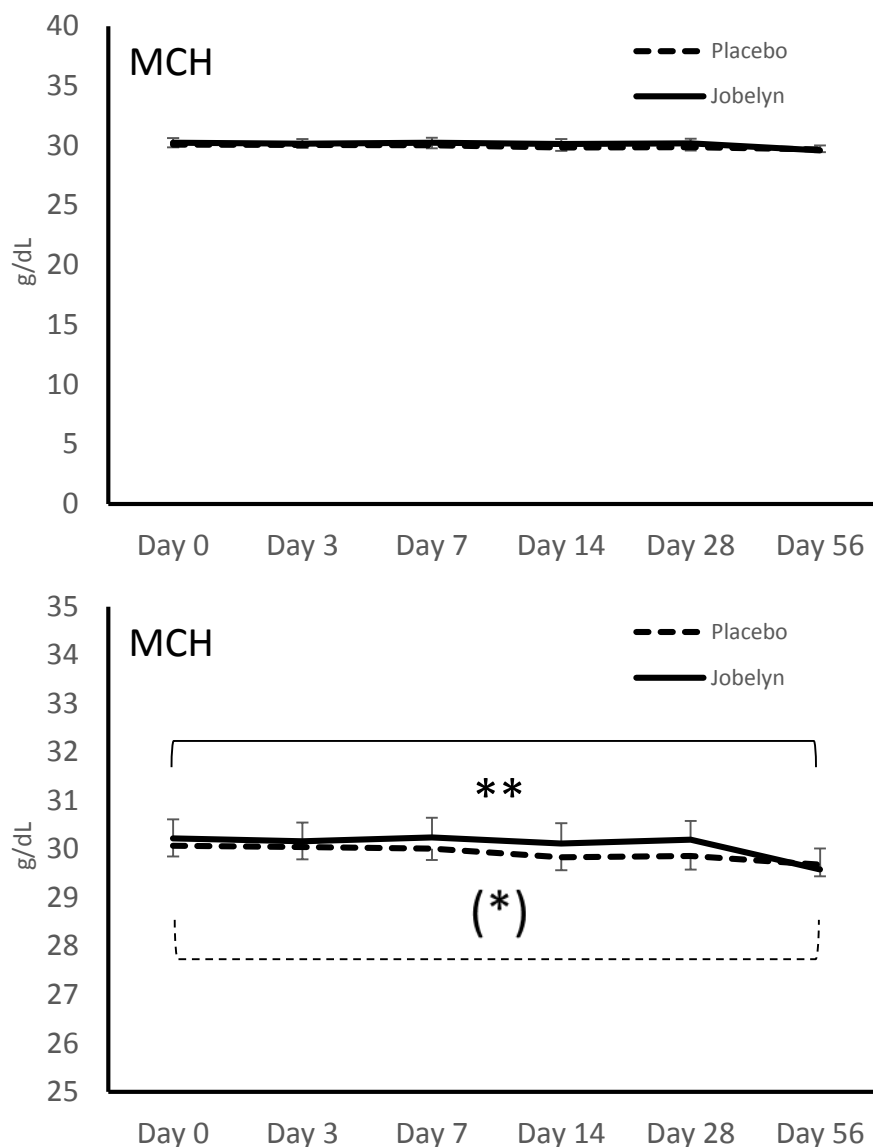


Figure 8. Mean corpuscular hemoglobin (MCH) is shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average MCH in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, minor fluctuations in MCH were seen in both groups. A very mild decrease in MCH was seen for the group consuming Jobelyn™ at Day 56 ($p < 0.01$, **) when compared to baseline for the Jobelyn™ group. ***This result may reflect that hemoglobin production (per cell) remained constant while the cell size slightly increased (MCV).***

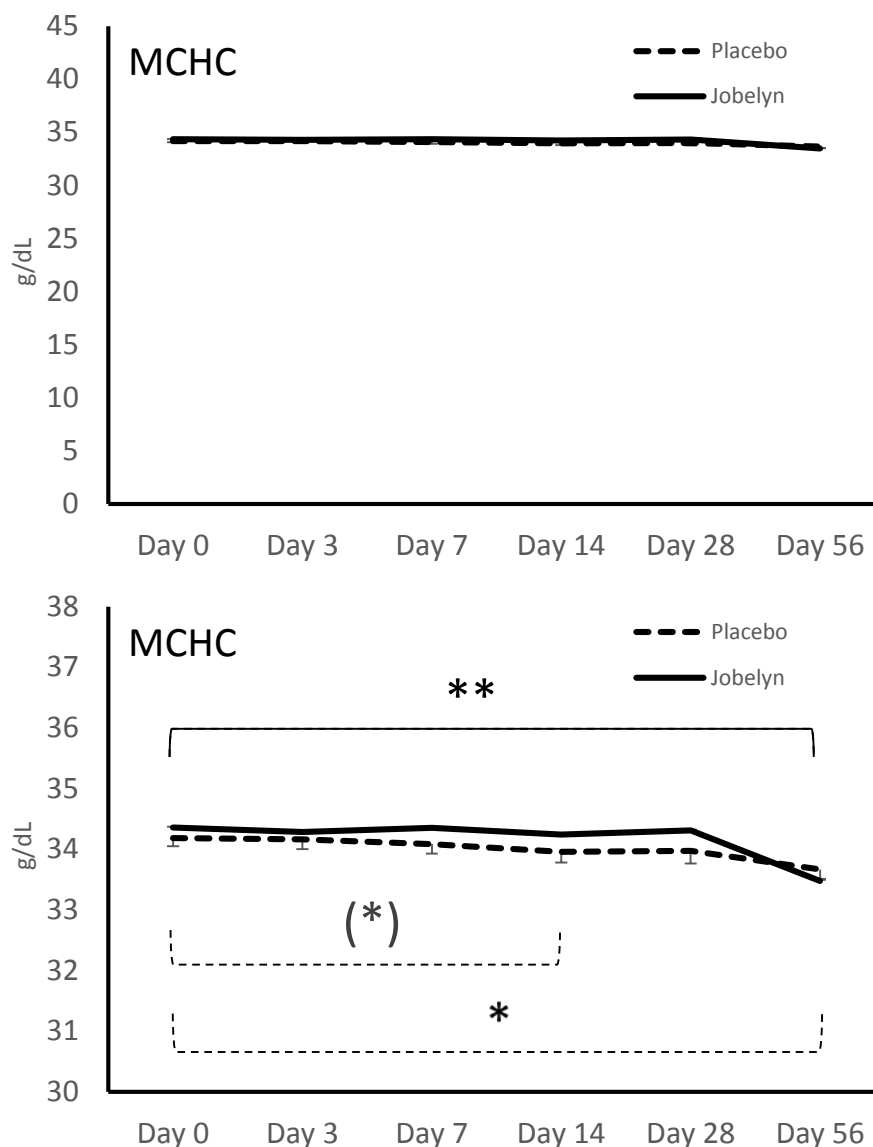


Figure 9. Mean corpuscular hemoglobin concentration is shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average MCHC in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, very minor decreases in MCHC were seen in both groups. This decrease was significant for the placebo group ($p < 0.05$, *), and highly significant for the Jobelyn™ group ($p < 0.01$, **) at Day 56 when compared to each respective baseline. ***This result may reflect that hemoglobin production (per cell) remained constant while the cell size slightly increased (MCV).***

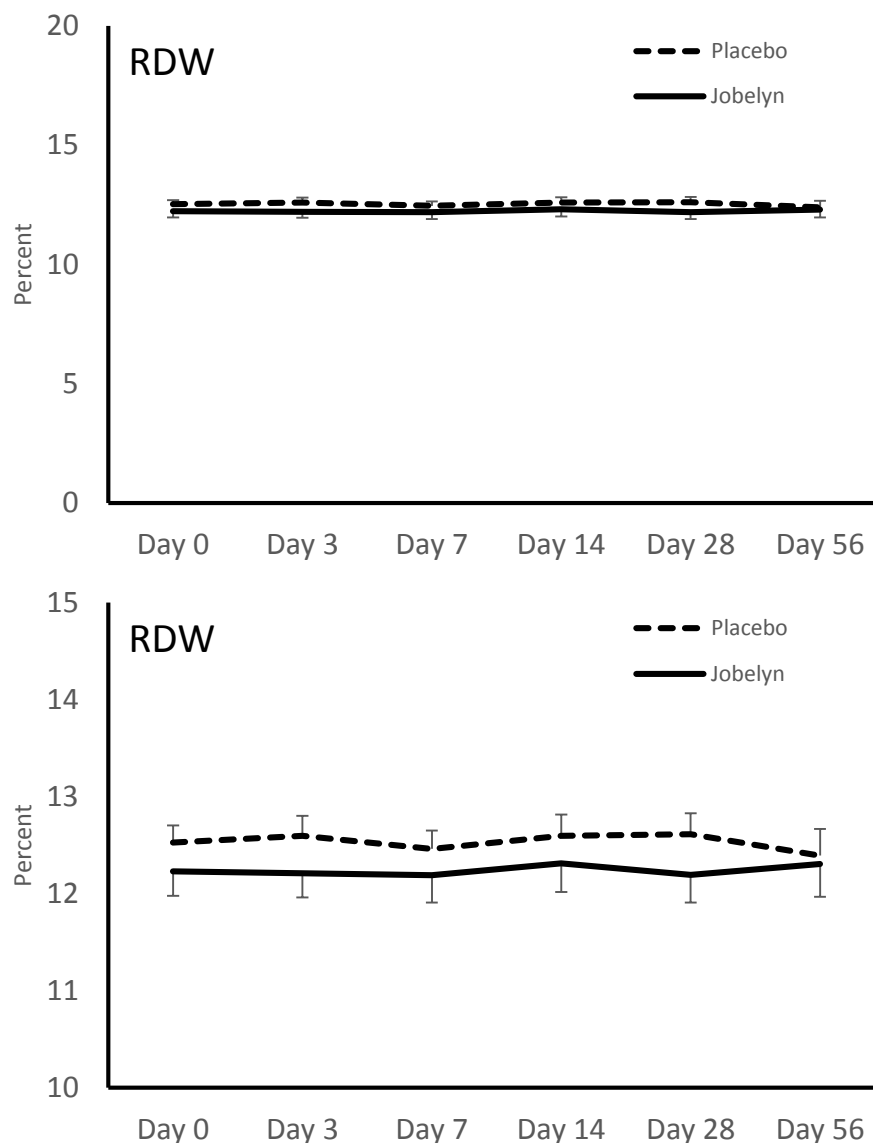


Figure 10. Red cell distribution width (RDW) is shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average MCHC in the placebo group and the Jobelyn™ group. The bottom graph serves to examine the data for any minor fluctuations. No significant changes were seen for either the placebo or the Jobelyn™ group, neither by *between-group* or *within-subject* analysis.

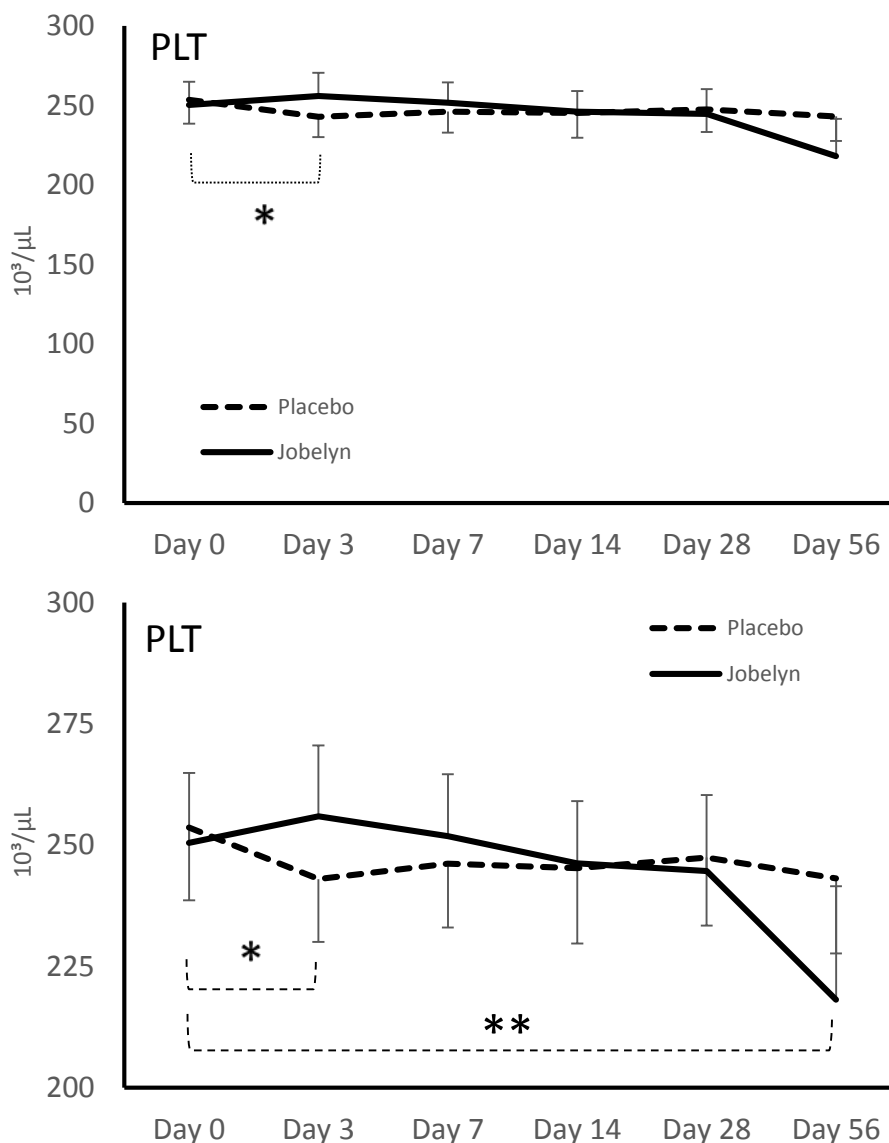


Figure 11. Platelet numbers (PLT) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to examine for differences between the average MCHC in the placebo group and the Jobelyn™ group at each time point. Interestingly, at Day 3, a significant difference was seen between the two groups, where a mild decrease in the placebo group, and a mild increase in the Jobelyn™ group resulted in significance between the Day 3 data ($p < 0.05$, *).

The bottom graph serves to illustrate that when ‘*within-subject*’ analysis was performed for each group separately, minor decreases in PLT were seen in both groups. This decrease was significant for the placebo group ($p < 0.05$, *) at Day 3, and highly significant ($p < 0.01$, **) at Day 56 when compared to baseline.

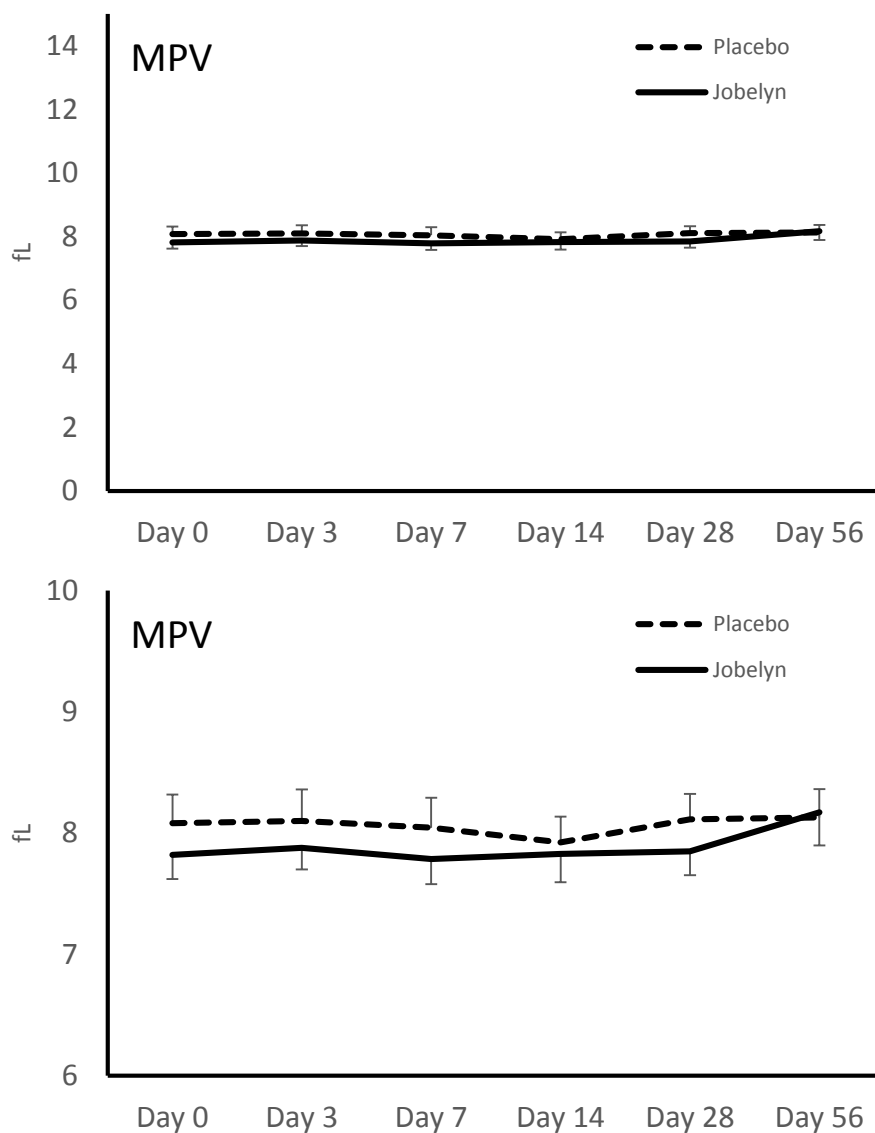


Figure 12. Mean platelet volume (MPV) is shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average MCHC in the placebo group and the Jobelyn™ group, using *between-group* statistical analysis. The bottom graph serves to examine the data for any minor fluctuations. No significant changes were seen for either the placebo or the Jobelyn™ group, using *within-subject* analysis.

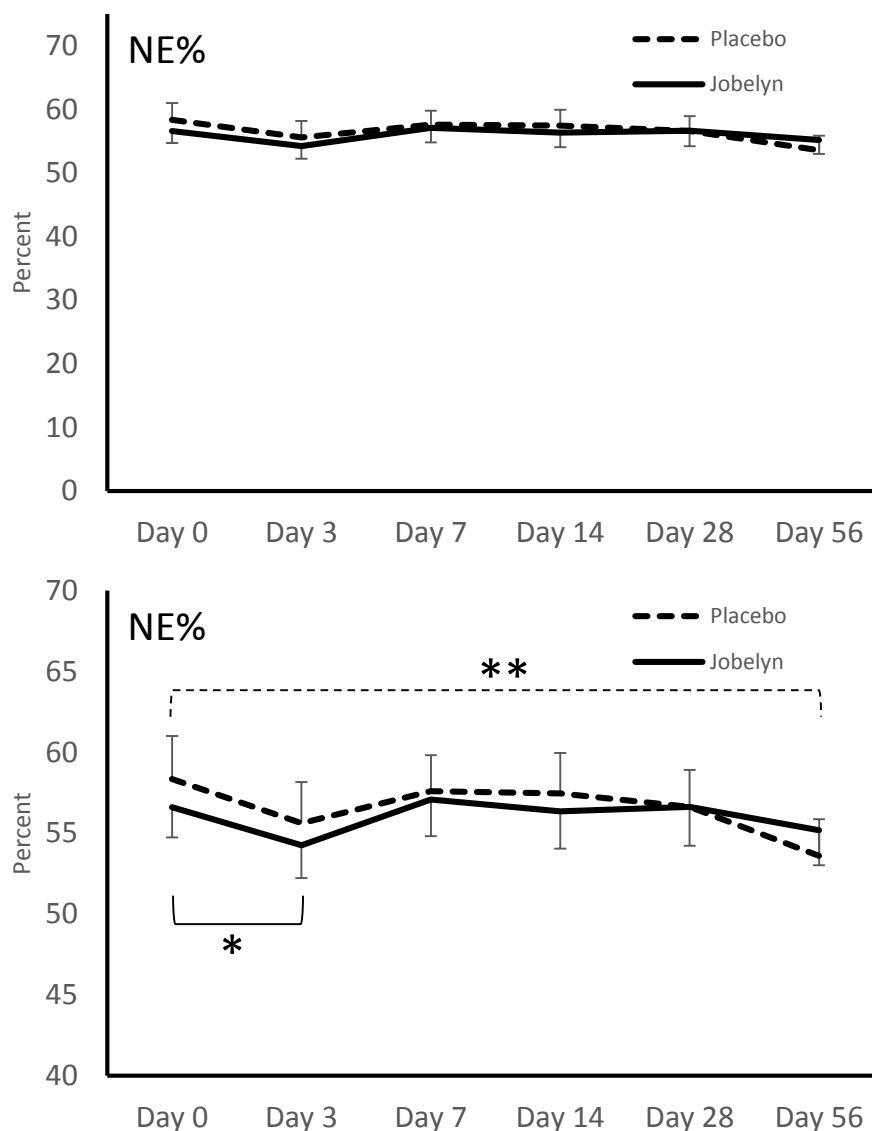


Figure 13. Neutrophil percentages (NE%) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average NE% in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, very minor decreases in NE% were seen in both groups. This decrease was highly significant for the placebo group ($p < 0.01$, **) at Day 56, and significant for the Jobelyn™ group ($p < 0.05$, *) at Day 3 when compared to each respective baseline. **The slow reduction in the placebo group may reflect seasonal changes. The apparent rapid change in the Jobelyn™ group needs to be evaluated in context of neutrophil numbers (NE#), see Figure 18, below. The combined data suggest that the rapid drop in NE%, while NE# remain constant, suggests a rapid increase of another white blood cell type.**

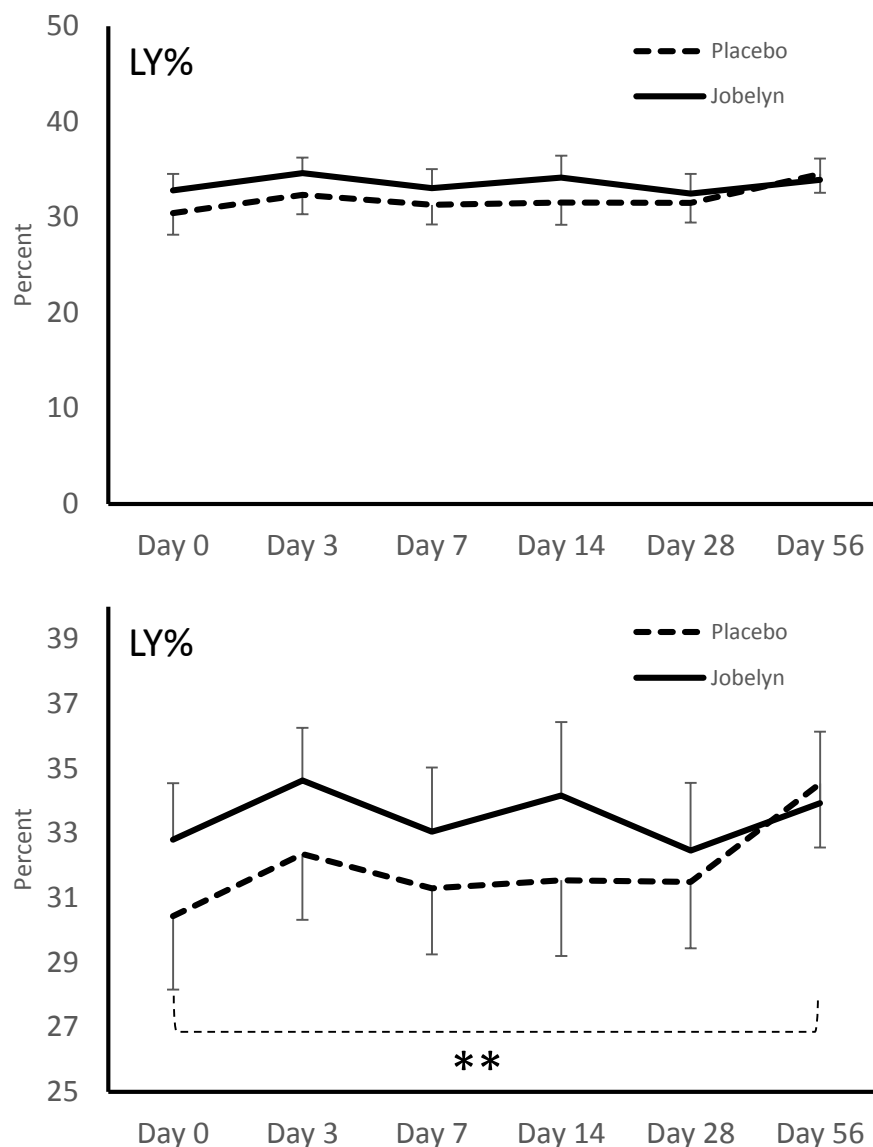


Figure 14. Lymphocyte percentages (LY%) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average LY% in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘*within-subject*’ analysis was performed for each group separately, very minor decreases in LY% were seen in both groups. This decrease was highly significant for the placebo group ($p < 0.01$, **) at Day 56 when compared to baseline.

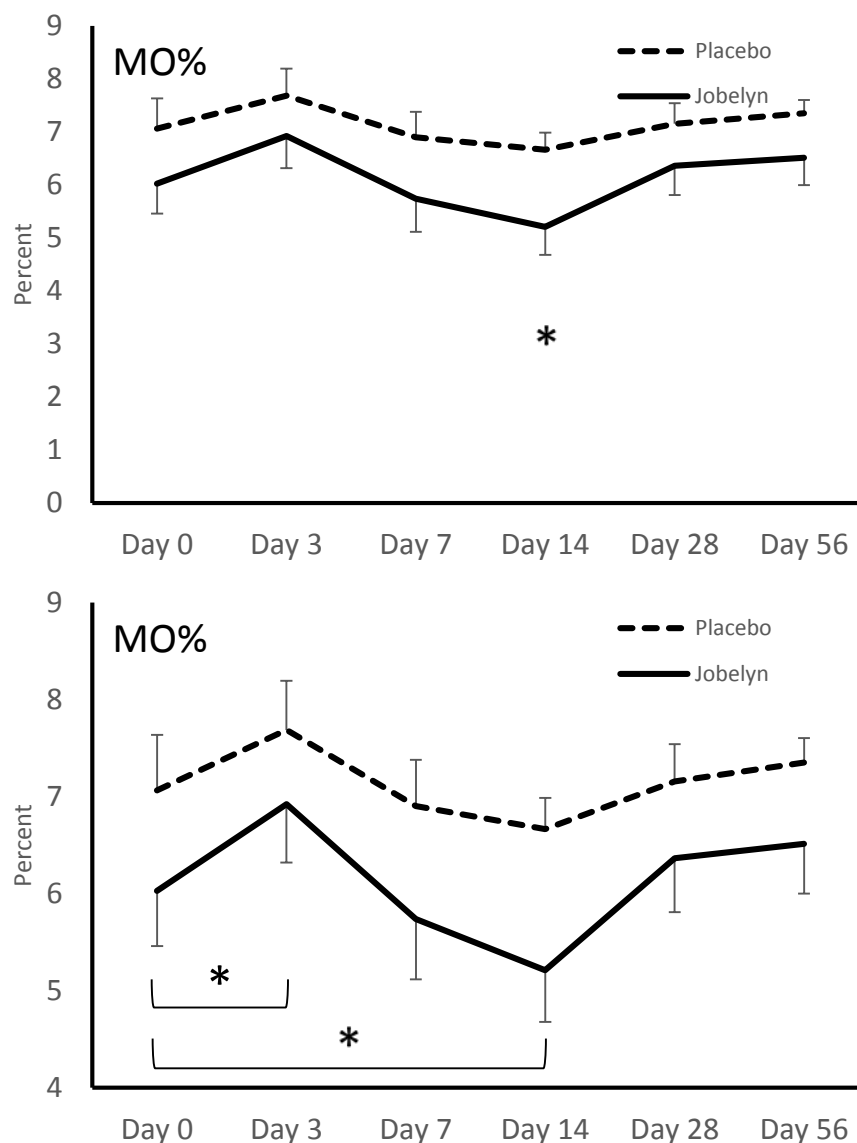


Figure 15. Monocyte percentages (MO%) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to examine for significant differences at each time point between the average MO% in the placebo group and the Jobelyn™ group. At Day 14, a significant difference was seen between the placebo and Jobelyn™ groups, where the Jobelyn™ group showed a transient decrease in MO%, compared to the placebo group at the same time point ($p < 0.05$, *). The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, two changes were noteworthy in the Jobelyn™ group. In the Jobelyn™ group, a rapid increase in MO% was seen at Day 3 ($p < 0.05$, *), followed by the reduction at Day 14 when compared to baseline. This is parallel to decreases in MO#, see Figure 20, below.

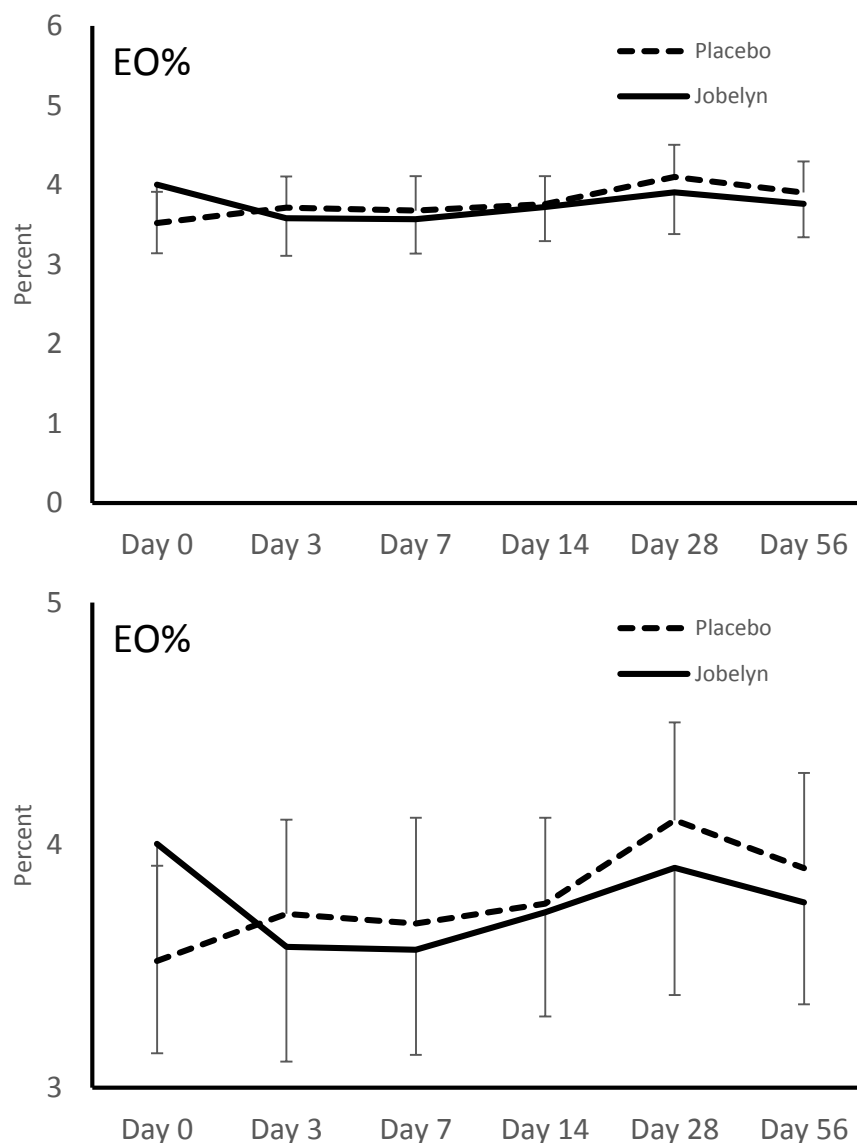


Figure 16. Eosinophil percentages (EO%) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average EO% in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when ‘*within-subject*’ analysis was performed for each group separately, there were no significant changes seen in either group. ***Interestingly, there was a rapid decrease in the Jobelyn™ group, already after three days of consumption.***

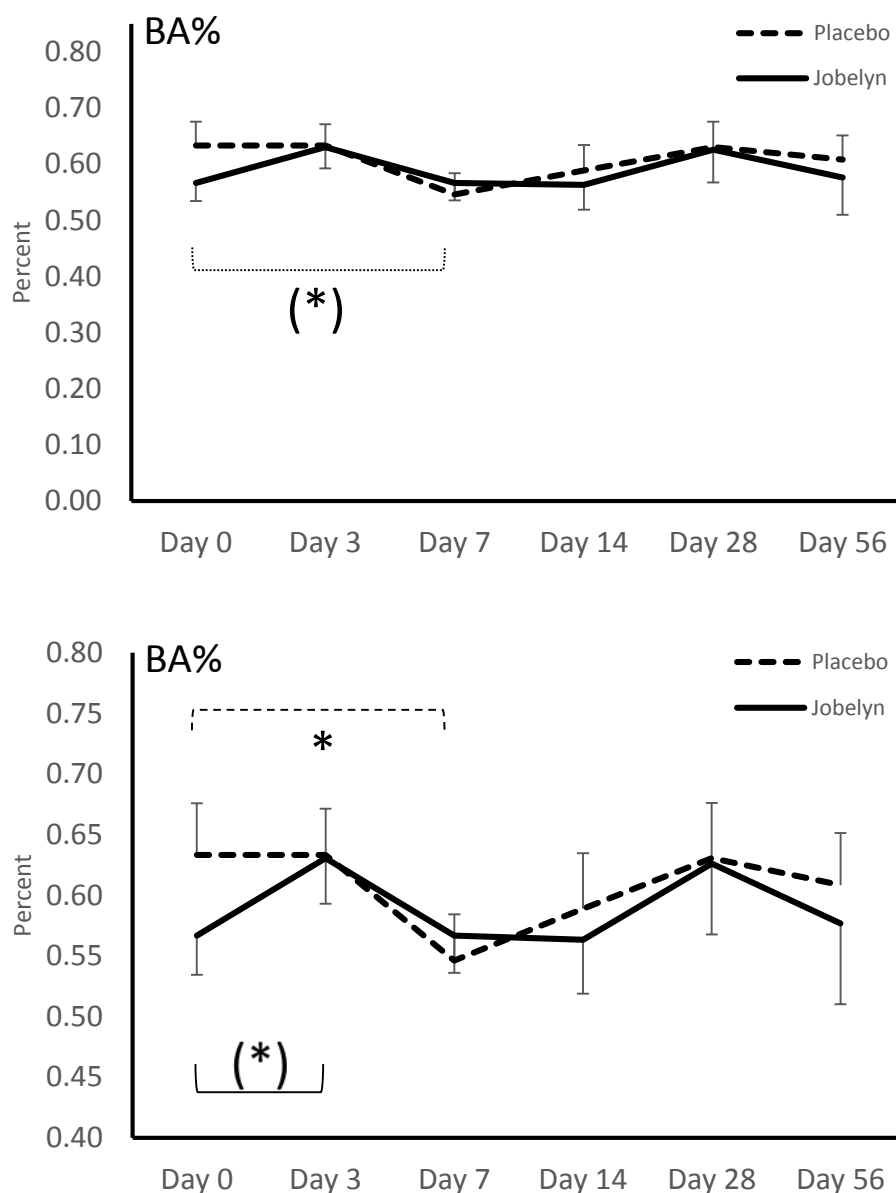


Figure 17. Basophil percentages (BA%) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average EO% in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, there were only very minor fluctuations in the BA% over the 8 weeks.

When evaluating this data, keep in mind the very low frequency of basophil cells. The normal range for BA% is 0-2%, so all data were minor fluctuations well within this normal range.

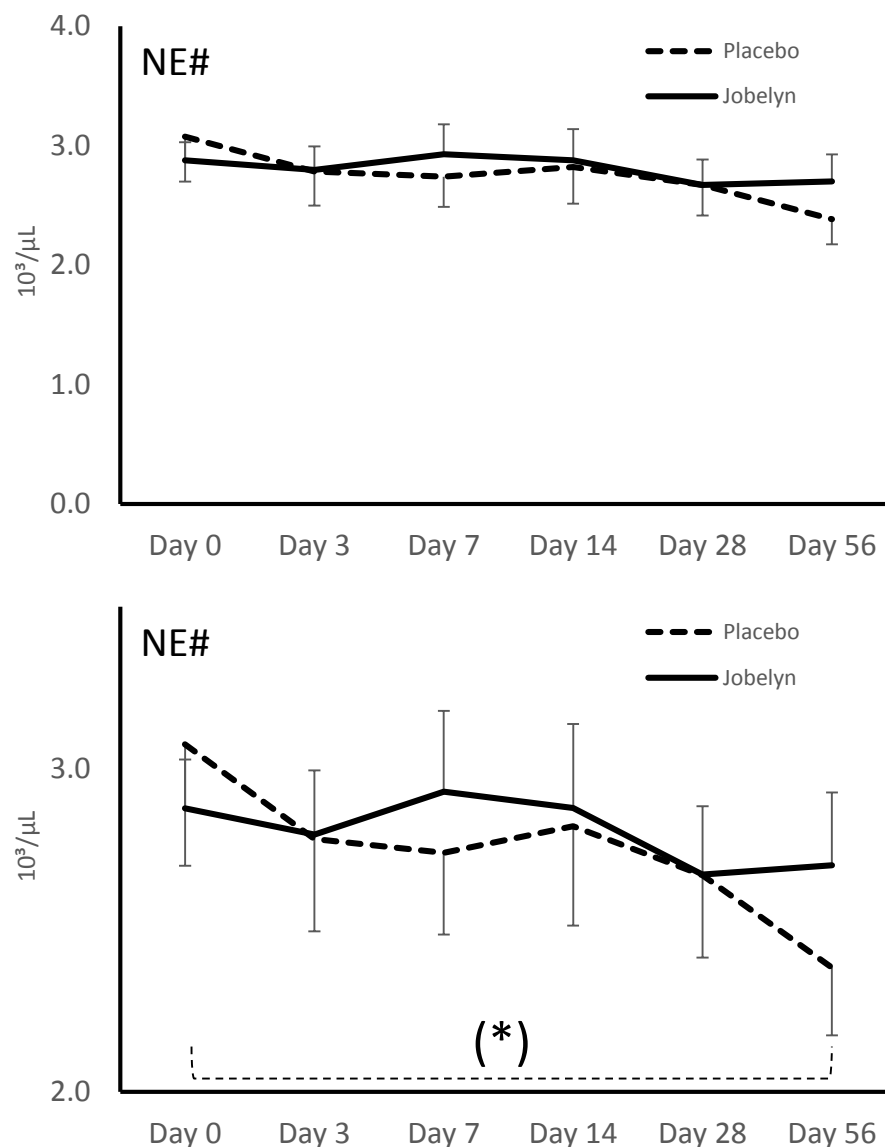


Figure 18. Neutrophil number (NE#) % are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average NE# in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, a minor decrease in NE# was seen in the placebo group. This decrease was trending towards significance ($p < 0.1$, (*)) at Day 56 when compared to baseline. **The slow reduction in the placebo group may reflect seasonal changes. The NE# remained more constant in the Jobelyn™ group over the 8-week period.**

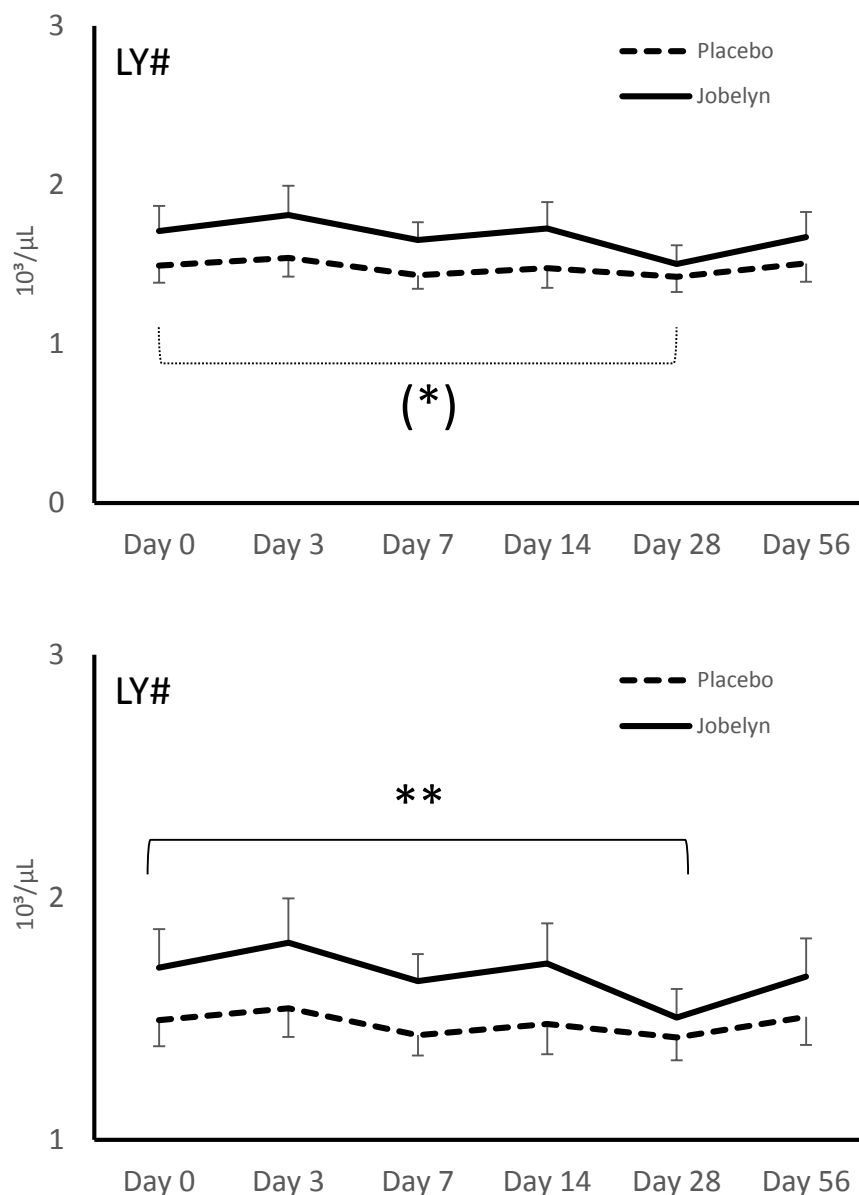


Figure 19. Lymphocyte number (LY#) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average LY# in the placebo group and the Jobelyn™ group. At Day 28, the mild reduction in the Jobelyn™ group was borderline significant ($p < 0.1$, (*)) when compared to the lack of changes in the placebo group over the same time period. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, the only noticeable change was the mild reduction in LY# in the Jobelyn™ group at Day 28 ($p < 0.01$, **).

Keeping in mind that the normal range for LY# in $1-4 \times 10^3/\mu\text{L}$ for males and $0.9 - 3.6 \times 10^3/\mu\text{L}$ for females, the fluctuations seen are very minor, and well within the normal range.

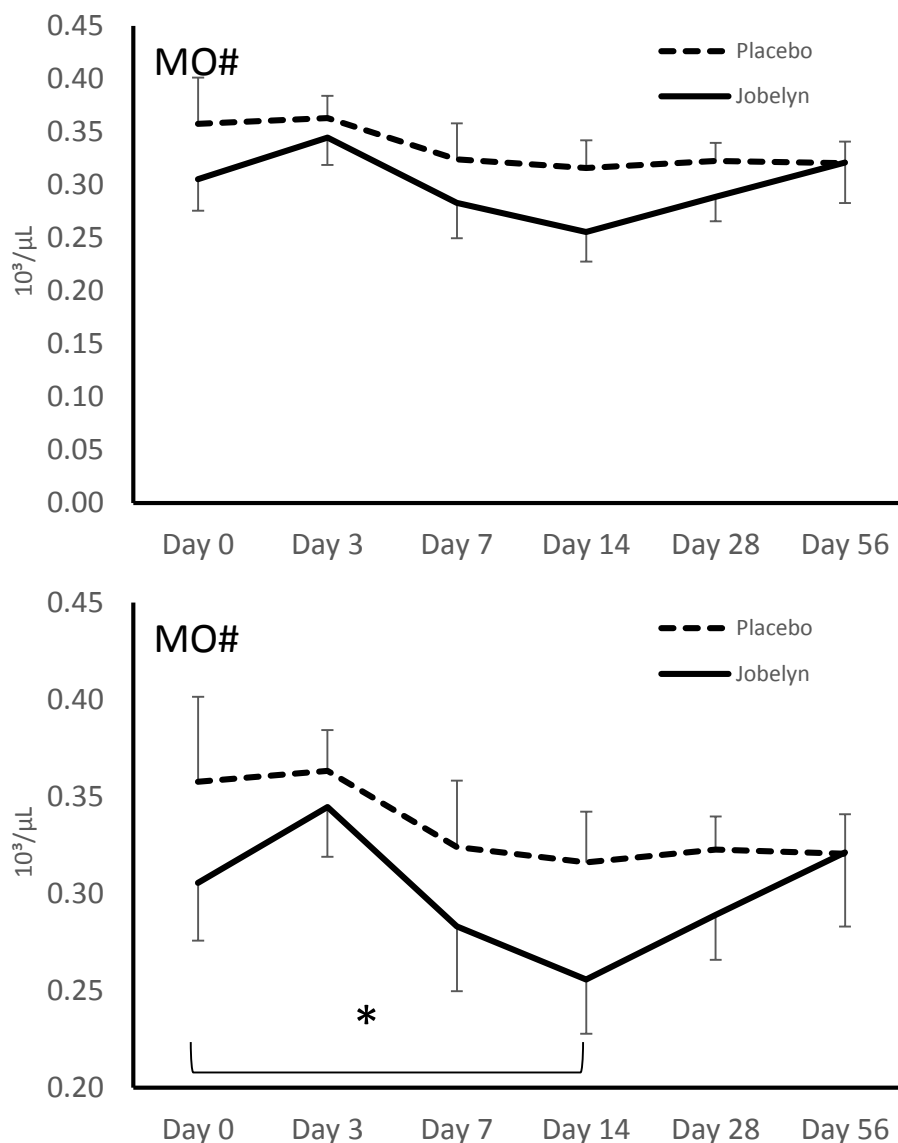


Figure 20. Monocyte number (MO#) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to examine for significant differences at each time point between the average MO# in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when 'within-subject' analysis was performed for each group separately, a rapid increase in MO# was seen at Day 3, followed by the reduction at Day 14 when compared to baseline ($p < 0.05$, *). The levels of MO# returned to baseline at Day 56. This is parallel to decreases in MO%, see Figure 15, above.

The fluctuations seen during the first 2 weeks of the study may reflect effects on Jobelyn™ consumption on monocyte numbers as part of increased immune surveillance, returning to pre-study levels after 8 weeks.

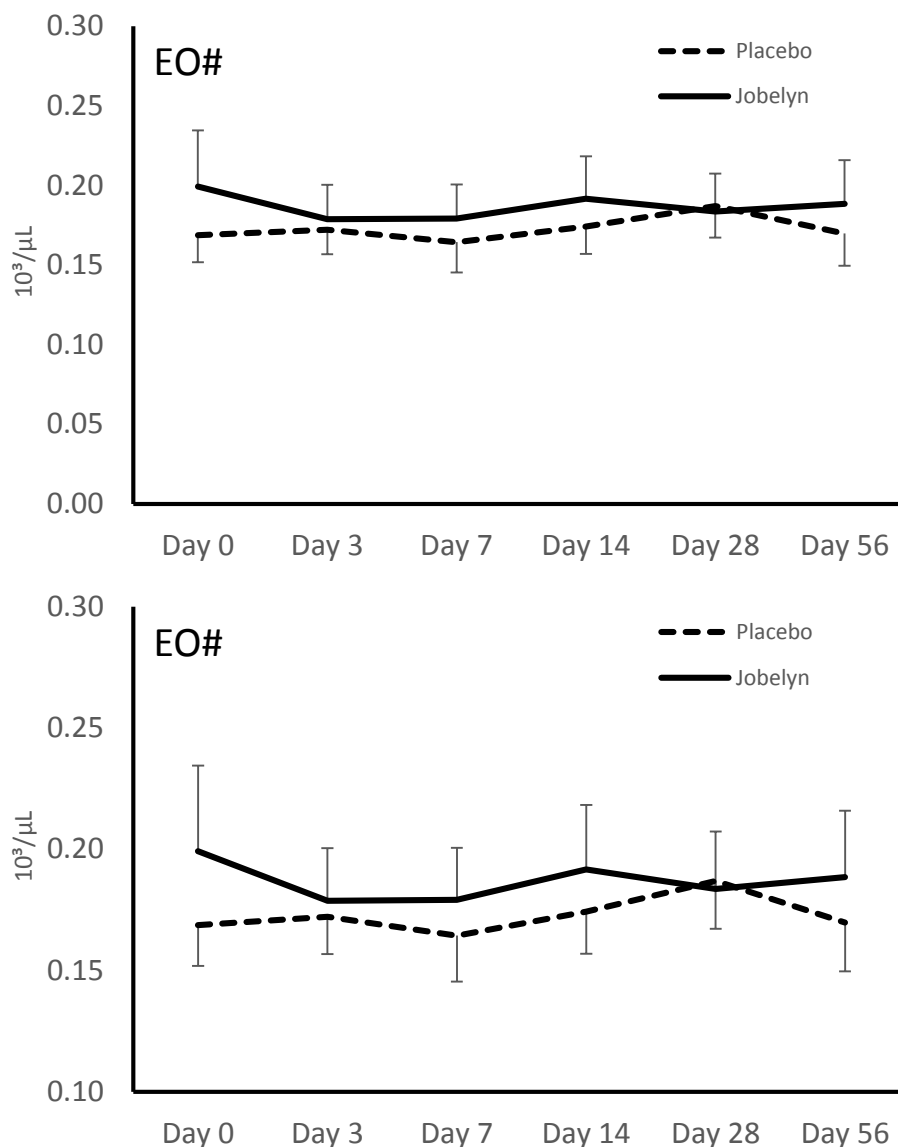


Figure 21. Eosinophil number (EO#) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average EO# in the placebo group and the Jobelyn™ group.

The bottom graph serves to illustrate that when 'within-subject' analysis was performed for each group separately, there were no significant changes seen in either group.

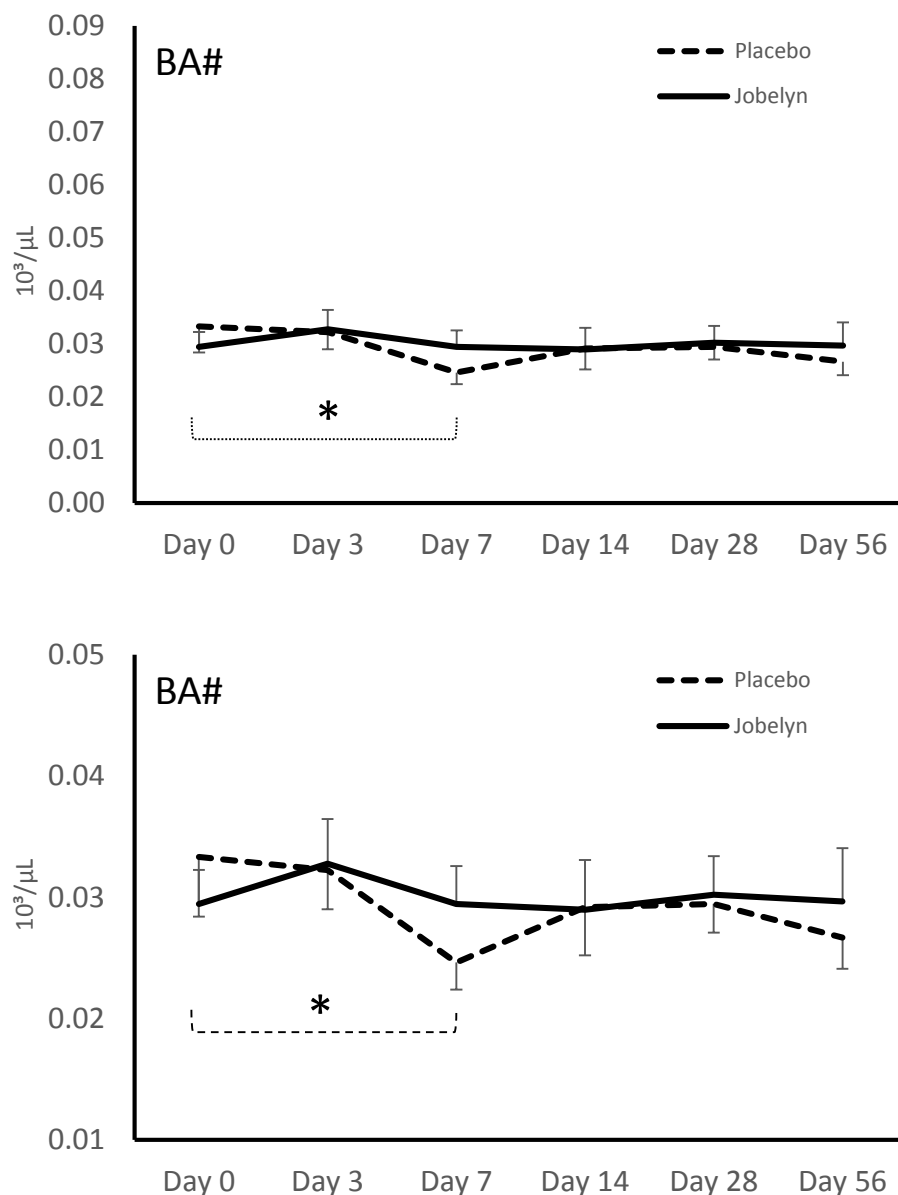


Figure 22. Basophil number (BA#) are shown as the group averages \pm SEM for each visit/blood draw. The top graph serves to illustrate that there were no significant differences at any time points between the average BA# in the placebo group and the Jobelyn™ group. The bottom graph serves to illustrate that when ‘within-subject’ analysis was performed for each group separately, there were only very minor fluctuations in the BA# over the 8 weeks.

When evaluating this data, keep in mind the very low frequency of basophil cells. The normal range for BA# is 0-0.1 x $10^3/\mu\text{L}$ %, so all data were minor fluctuations well within this normal range.

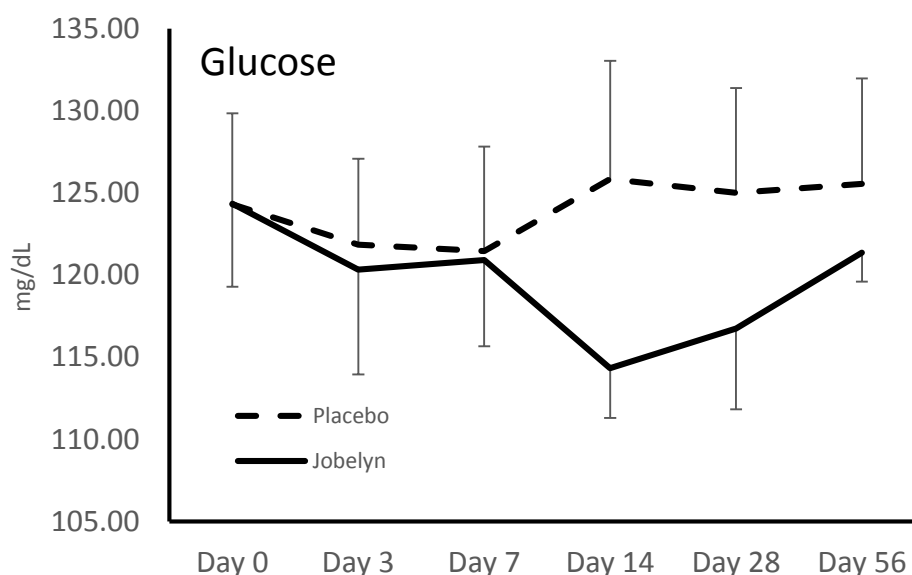


Figure 22. Fasting blood glucose levels are shown as the group averages \pm SEM for each visit/blood draw. The baseline levels of fasting blood glucose were similar in the placebo and the Jobelyn™ groups, and showed that the study population overall was pre-diabetic with an average fasting blood glucose level above 110 mg/dL. There were no significant differences at any time points between the average fasting glucose levels in the placebo group and the Jobelyn™ group. Even though there were no statistically significant differences, it is interesting that the group consuming Jobelyn™ showed lower fasting glucose levels than the placebo group from Day 14 and during the rest of the 8-week study.

Conclusions

Safety

The data presented here helps document basic safety aspects of Jobelyn™ consumption in a North American population. The rapid changes in red blood cell numbers and T cell numbers in West African studies in HIV+ populations could raise the question whether Jobelyn™ consumption is safe to consume for people who have close to normal numbers of such cell types, and whether Jobelyn™ consumption may trigger cellular production in the bone marrow that may be out of control. The data presented in this report clearly documents that Jobelyn™ consumption does not trigger such unhealthy production of cells. This can be seen as an important part of Jobelyn™'s safety data portfolio.

The highly specific activation of immune cells, documented in vitro [Benson et al. 2013], could lead to safety related concerns, such as whether Jobelyn™ consumption may trigger over-activation of immune reactions. The current data presented in this report does not suggest such events. Rather, the changes seen were either normalizing or transient, suggesting that Jobelyn™ consumption supports a healthy normalization of many aspects of red and white blood cell production and function.

Red blood cell health

Previous and ongoing studies in West Africa have seen very rapid improvement in RBC status, including improvements in hemoglobin in an HIV+ population. The data from these studies were performed in study populations where some common health challenges affecting RBC health include sickle cell anemia and parasitic infections such as malaria, i.e. conditions associated with accelerated RBC senescence and clearance.

In the study performed at NIS Labs, quite different results were obtained. Several factors may help explain this data in context of the West African studies. We suggest that the very mild, but highly significant changes seen in all parameters of RBC health, associated with consumption of Jobelyn™, may be associated with the following:

- Jobelyn™ activation of RBC production, leading to increased production of new RBC that are slightly larger than senescent RBC, thereby affecting RBC mean cell volume;

- Jobelyn™ activation of macrophage function, leading to a better clearance of senescent RBC over time;

These mild changes in relative cell numbers seen associated with Jobelyn™ consumption should be interpreted with an open mind, since there are several unknown factors. The data should be considered in context of overall effect on bone marrow function and production of many different cell types.

An alternative suggested explanation of the reduced RBC numbers may be if Jobelyn™ has negative effects on iron absorption – however, this goes against the West African data where a much more challenged population saw huge benefits. Alternative explanations include production of healthier RBC with a proper senescence process, and healthier clearance of senescent RBC by spleen macrophages.

It is also possible that an ‘overworked’ bone marrow at high altitude and chronic low-grade inflammation may have been the status of the recruited subjects, where Jobelyn™ consumption allowed the marrow to produce a slightly lower amount of red blood cells of a higher quality, and redirect bone marrow efforts to an increased production of immune cells as needed (such as the increase in platelets and monocytes by Day 3).

Whether this also allowed the bone marrow to increase the production of stem cells was not answered by this study, but could be addressed in future studies.

Interestingly, the population was pre-diabetic, as almost the entire population started the study with fasting glucose levels at 100 mg/dL or above. The association between circulating glucose levels and anemia is illustrated by the prevalence of anemia in a large proportion of diabetic patients.

Immune cells

Several observations are of interest here.

A rapid increase in monocytes was seen at Day 3, followed by a slight decrease at Day 14, after which time the monocyte percentage and numbers returned to baseline levels. This suggests that the initial consumption of Jobelyn™ initiated an immune response to latent or potential pathogens, which a slightly compromised immune system had been unresponsive to. (The elevated fasting glucose levels and borderline anemic conditions are suggestive of a possible association with mild systemic stressors, including low grade chronic inflammation).

Changes were seen in the platelet numbers in the placebo group, where a slight reduction happened across the 8-week study period. In contrast, the platelet levels in the Jobelyn™ group showed a mild increase at Day 3. This increase became statistically significant with the removal of one outlying data set, such that at Day 3 there was a significant difference in platelet numbers between the placebo and the Jobelyn™ group. This supports the suggestion of a rapid effect of Jobelyn™ on bone marrow production of various cell types. Interestingly, the progenitor stem cells that differentiate into red blood cells are shared with the progenitor path that leads to production of platelets and monocytes.

Fasting blood glucose

The study population was almost entirely comprised of pre-diabetic people with a fasting glucose level of 100 mg/dL or higher at study start. This was not associated with obesity, as many study participants had low-normal range BMI.

The measure of fasting glucose levels during this study aimed at collecting pilot data on whether Jobelyn™ consumption would be associated with regulation of fasting blood glucose. No significant changes were seen. There were a few cases where a drop in fasting glucose levels was seen at day 3 compared to baseline. Further study of the effects of Jobelyn™ consumption on fasting blood glucose is warranted, also in overweight and obese people.

Recommendations for future studies

The following options for further work may help increase our understanding of Jobelyn™ on regenerative functions, including red blood cell production and immune status:

- 1) Testing of comprehensive cytokine profile on the banked serum samples from this study may point to mechanisms that could further explain the data presented in this report; this may for example include the increased production of anti-inflammatory, immune regulatory, and stem cell supportive cytokines;
- 2) A study of longer duration, allowing us to follow RBC levels and quality for at least the 120 day typical life span of RBC;
 - a. Study would examine markers for RBC senescence;
 - b. Study would drill into more detail regarding immune cells:

- i. Even though lymphocyte numbers seemed constant in both groups, it is possible that subsets of T and B lymphocytes were changed in the Jobelyn™ group, compared to the placebo group;
 - ii. This may include important changes within the lymphocyte population, for example involving T regulatory cells and natural killer cells, as well as antigen-presenting monocyte/macrophage and dendritic cell types.
- 3) Study may address other cell types, such as circulating stem cells.

References

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