A randomized-controlled clinical study of Telos95®, a novel antioxidative dietary supplement, on the shortening of telomere length in healthy volunteers

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Abstract

Introduction: The objective of this study was to determine the deodorant effectiveness of a dietary supplement to halt the shortening of telomere length as measured through blood samples before and after product use.

Patients and methods: This study was a randomized controlled design in fifty (50) healthy adult subjects. Qualified subjects provided a small blood sample via finger stick at their baseline visit. The blood samples were sent to Telomere Diagnostics Inc. for analysis of telomere length which is used to calculate average telomere length (ATL). Subjects were randomized into one of two treatment groups: test article once per day (group A) or twice per day (group B). Subject were provided the test article, a diary to ensure compliance and instructions for use of the test product.

Results and discussion: A total of fifty (50) subjects completed all aspects of the study. Group A decreased in their TeloYear age on average by 7.43 years. Group B decreased in their TeloYear age by 8.52 years. Average telomere length (ATL), also represented as the T/S ratio, showed a baseline measurement of 0.85 but after taking the product for 6 months it increased to 0.95. Group B baseline ATL measured 0.82 at baseline and increased to 0.94 post 6 months of test article usage.

Conclusion: These results suggest that Telos95® supplementation can be an effective and safe approach to halt the shortening of telomere length.

Key words: antioxidative, clinical study, dietary supplement, telomerase, telomere, Telos95, randomized-controlled.

Introduction

Telomeres are functional complexes at the base of eukaryotic chromosomes. They help to maintain and prevent deterioration of the cells[1]. Shorter telomeres have been shown to be the cause of aging and become shorter due to the aging process and an unhealthy lifestyle[2]. The shorter the telomere becomes, the less it can prevent cell death due to the cell no longer being able to divide properly[3].

Telomerase consists of RNA subunits and proteins which aids in elongating telomeres. This lengthening process occurs by adding DNA base-pair sequences to the ends of chromosomes[4].

The objective of this study was to assess the efficacy of a dietary supplement to prevent the telomere shortening when taken over a six-month period. The study compared the baseline telomere results for subjects to results obtained after six months of test article usage[5].

The analysis measures individual's average telomere length (ATL) and provides a "TeloYear" age based on how the subject's Average Telomere Length (ATL) compares to others of the same age and gender[6].

Patients and methods

Selection of Subjects

Screening

An adequate number of subjects were screened and enrolled so that a minimum of 50 subjects would complete the study. Subjects had to satisfy the following inclusion and exclusion criteria, and had to give written informed consent.

The suitability of each subject to participate was confirmed prior to their acceptance onto the study by completion and review of a study specific inclusion and exclusion criteria as well as an assessment by the expert grader and subjective assessments.

Inclusion criteria

a. Healthy volunteers, 30 to 60 years of age;
b. Completed written informed consent containing HIPAA authorization.

Exclusion criteria

a. Female subject is pregnant, nursing or planning to become pregnant (Verbal response only)
b. Subject is an insulin-dependent diabetic.
c. Subject has a disease which, in the opinion of the Investigator, would compromise the safety of the subject or the validity of the study outcome.
d. Subject has a heart condition or a history of heart issues, which, in the opinion of the Investigator, would compromise the safety of the subject or the validity of the study outcome.
e. Subject has a medical history which, in the opinion of the Investigator, would compromise the safety of the subject or the validity of the study outcome.
f. Subject has a history of any malignancy or tumor.

Prohibitions and Restrictions for the Duration of the Study

a. Subject agrees to attend all test facility appointments and follow all study instructions.
b. Subject agrees not to use any antioxidant supplements or dietary supplements that are intended for telomere enhancements for the duration of the study.

Subject Withdrawal

The participation of a subject in this study may have been discontinued for any of the following reasons:

- An adverse event that requires study article to be discontinued;
- Withdraws consent to continue participation in the study;
- Protocol violation (including lack of compliance);
- Other reasons, such as administrative reasons.

Subjects who prematurely dropped out of the study were not replaced.

Test articles

The test article was: Telos95® Dietary Supplement.

Table 1. Parameters of randomization.

Randomization – Amount of Daily use of Test Article	
A	Usage of product once a day (1 capsule of 95 mg each)
B	Usage of product twice a day (2 capsules of 95 mg each)

The test article was used according to the use instructions.

Study procedure

Visit 1 – Screening

A sufficient number of were screened and enrolled on to the study to ensure that a minimum of 50 subjects completed all phases of the study. Qualified subjects had a small blood sample collected via finger stick using the telomere diagnostic collection kit provided by the diagnostic lab (Telomere Diagnostics Inc.). Subjects were assigned to one of two treatment groups (A or B) according to the randomization. Group A was instructed to take one capsule once a day, preferably with a meal. Group B was instructed to take one capsule twice a day, one capsule in the morning and one capsule in the evening and each preferably with a meal. Blood sample collection kits were sent to Telomere Diagnostics Inc. for analysis. The test products were to be taken daily at home for the following 6 months of the study according to the usage instructions provided. Subject were given a diary to fill out every day each time they took the product.

Visit 2 – Month 6 – End of Study

Subjects returned to the test facility following six months of test product use. Adverse events were reviewed and recorded. Subjects were asked to return any unused test product including empty

bottles. Subject compliance with the study instructions and restrictions were assessed and completed diaries were reviewed. A second blood sample (via finger stick) was collected from each subject using the telomere diagnostic collection kit. These samples were sent to the diagnostic lab (Telomere Diagnostics Inc.) for analysis. After the visit was completed, the subject's participation was considered final and they were compensated for their participation.

Study Evaluations

Blood samples (via finger stick) were collected using a collection kit provided by the telomere analysis lab. Samples were collected at baseline and sent to Telomere Diagnostics Inc. for analysis. After 6 months of test article use (either once a day or twice a day) subjects returned to PCR for blood sample collection. Blood samples Analysis of the telomere to determine the average telomere length (ATL) was conducted using the Cawthon qPCR assay.

The basic theory is that the ratio of the telomeric signal vs. the single copy gene signal reflects the average length of the telomeres per cell in the sample (Telomere Diagnostics, Inc.). The results of the ATL were used to assign a TeloYear age to each subject based on the comparison of their ATL to others in their same age and gender.

Study ethics

Ethical Conduct

This study was conducted in compliance with applicable Good Clinical Practice (GCP) Regulations, the Standard Operating Procedures of Princeton Consumer Research and the Sponsor's Protocol and Protocol Amendments.

The Sponsor was responsible for the ongoing safety evaluation of the investigational products and will promptly notify participating Investigators and regulatory authorities of findings that could have adversely affected the safety of subjects, impact the conduct of the study, or alter the IRB's approval to continue the study.

Subject Information and Consent

Subject consent was obtained prior to participation in any study conduct as required by the regulatory guidelines (21 CRF Part 50). Subjects were given ample opportunity to read the consent form and have all questions regarding study conduct answered prior to signing the consent form. Each subject was provided with a copy of the ICF to retain for his or her records. The original signed ICF was retained on file at the study center.

Authorization to Disclose Protected Health Information

Subjects were informed of the following information: The purpose of the protected health information (PHI) being collected, the possibility that the PHI may be re-disclosed, the duration of the authorization, the right to revoke the authorization, and the right to refuse signature and limit access to PHI during and following the conduct of the trial. Written authorization to disclose PHI was incorporated into the informed consent process and was obtained prior to the subjects entering the study per Princeton Consumer Research standard operating procedures (SOPs). Each subject was provided with a signed copy of the authorization and the original was retained on file at the study center.

Indemnity provision

The Sponsor was responsible, without regard to legal liability, and would indemnify Princeton Consumer Research Corp., or any of their respective officers or employees in the event of claims for compensation from subjects suffering injury or other deterioration in health or wellbeing as a result of participation in this study, except and insofar as such claims arise as a result of any negligent act or omission on the part of Princeton Consumer Research Corp. employees or any persons undertaking or involved in the study by arrangement with Princeton Consumer Research Corp.

Results and discussion

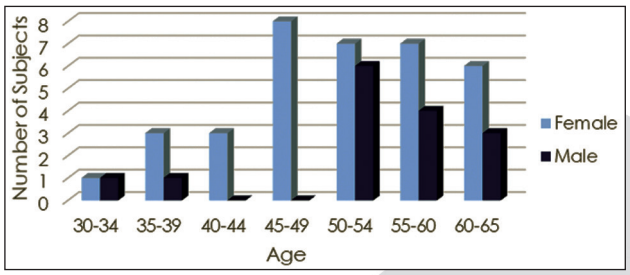
Study data

Location and dates of the study

The study was conducted according to the protocol at Princeton Consumer Research Corp. from 23 March 2017 to 25 April 2018. The original screening was on 23 Mar 2017. The subjects were reconsented and additional subjects were screened and consented for those subjects that didn't reschedule their second visit on 24 Oct 2017.

Subjects

Fifty-nine (59) subjects were screened and enrolled and fifty (50) subjects completed the study. The graphic 1 shows the subjects demographics details.



Graph 1. CERTEL1F Demographics

Adverse Events and Severe Adverse Events

There was one Serious Adverse Event on the study that was not related to the Test Product. Subject 45 was hit by a car and was admitted to the hospital. She suffered a broken pelvic bone and a fractured femur.

Discontinued Subjects

Twenty-six (26) subjects discontinued participation on the study. The table above shows the details on discontinued subjects.

Table 2. Discontinued subjects.

Subject number	Reason for discontinuation
09, 29	PI dropped due to medical history
06	Subject withdrew consent
11, 12, 13, 14, 16, 17, 20, 21, 22, 27, 34, 35, 36, 43, 47, 48, 51, 52, 55, 58, 73, 80	Lost to follow-up. Unable to attend all visits.
49	Subject dropped due to actions on another study. Subject no longer allowed to participate in studies at PCR Corp.

Average TeloYears age decrease

Group A decreased in their TeloYear age on average by 7.43 years. Group B decreased in their TeloYear age by 8.52 years. The tables below show the details on age decrease in both groups.

Table 3. Decrease in TeloYears Age.

Subject number	Group A
2	-11
3	-3
4	1
18	-4
26	-21
32	0
37	-4
38	-13
40	-12
44	-9
45	-6
46	-30
53	1
54	-10
59	-27
61	0
65	-22
74	18
75	-20
77	0
79	1
81	0
82	0
Average	-7.43

Subject number	Group b decrease in teloyears age
1	0
5	-23
7	1
8	2
10	-21
15	0
19	-12
23	15
24	0
25	-1
28	-30
30	-17
31	-28
33	-8
39	0
41	-12
56	0
57	-11
62	-24
63	0
64	-11
66	-7
68	0
70	0
71	-22
76	6
78	-27
Average	-8.52
P value	7.42E-01

Conclusion

A total of fifty (50) subjects completed all aspects of the study. Group A decreased in their TeloYear age on average by 7.43 years. Group B decreased in their TeloYear age by 8.52 years. Average telomere length (ATL), also represented as the T/S ratio, showed a baseline measurement of 0.85 but after taking the product for 6 months it increased to 0.95. Group B baseline ATL measured 0.82 at baseline and increased to 0.94 post 6 months of test article usage.

References

1. *Punder K, Heim C, Wadhwa PD, Entringer S. Stress and immmunosenescence: the role of telomerase. Psychoneuroendocrinology, 2018; 101: 87-100.*

2. *Ullah M, Sun Z. Klotho deficiency accelerates stem cells aging by impairing telomerase. The Journal of Gerontology A, 2018; 18: 08-27.*

3. *Palsgrove DN, Taheri D, Springer SU, Cowan M, Guner G, et al. Target sequencing of Plasmacytoid urothelial carcinoma reveals frequent TERT promoter mutations. Human Pathology, 2018; 14: 28-35.*

4. *Hornsby PJ. Telomerase and the aging process. Experimental Gerontology, 2007; 42: 575-581.*

5. *Bar C, Blasco MA. Telomeres and telomerase as therapeutic targets to prevent and treat age-related diseases. F100Research, 2016; 89: 1-11.*

6. *Shay JW. Role of telomeres and telomerase in aging and cancer. Cancer Discovery, 2016; 6(6): 584-593.*

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