International Journal of Clinical Trials
Gadani MC et al. Int J Clin Trials. 2024 May;11(2):109-116
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: https://dx.doi.org/10.18203/2349-3259.ijct20240303

Original Research Article

Anti-ageing effects of CollabZen™ in healthy human volunteers: a randomized, double blind, placebo-controlled study

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Received: 15 January 2024
Revised: 25 January 2024
Accepted: 31 January 2024

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ABSTRACT

Background: There are several concerns related to combating signs of ageing. Considering the long-term safety concerns of cosmetic formulations, a safe and effective approach using nutritional supplements and naturals should be of great help. CollabZen™ is one such a blend of three plant materials known as *Phyllanthus emblica*, *Camellia sinensis*, and *Coffea arabica,* earlier tested for collagen building in human cells *in-vitro.* The current study aims to explore its potential as a nutraceutical product for skin ageing.
Methods: The study enrolled 64 volunteers both genders (mean age=45.75) with crow's feet wrinkles. One group (n=32) received a placebo capsule (Product A) and other group received CollabZen™ capsules (Product B). Dermatological parameters were assessed at 0th day, 4th and 8th week, and self-assessment questionnaires for efficacy and tolerance were collected on 4th and 8th week. The trial is registered at https://ctri.nic.in/, CTRI/2022/10/046168.
Results: The results showed that product B (CollabZen™) was significantly effective than the placebo in improving deep skin hydration on the face (p=0.009), increasing facial skin elasticity (p=0.001), and enhancing firmness (p=0.001) after 8 weeks. Participants in Group B reported higher levels of satisfaction regarding their perceived skin health compared to group A based on self-assessment at the 8th weeks (p<0.01). Moreover, only one volunteer in each group experienced mild intolerance at the end of 8th week, demonstrating the safety of these nutraceutical ingredients and excipients.
Conclusions: CollabZen™, with its known antioxidant and collagen-boosting properties and current findings can be considered a valuable nutraceutical product for the anti-ageing sector of the cosmetic industry.

Keywords: CollabZen™, Nutraceuticals, Skin ageing, Nutrition, Phytocompound

INTRODUCTION

The skin, being the body's largest organ and primary defence mechanism, undergoes constant ageing due to either internal factors (programmed ageing) or external factors (accelerated ageing) such as sunlight, pollution, lifestyle choices, and hormonal imbalances.[1] Throughout history, the connection between nutrition and skin health has been well-understood and adopting a well-regulated lifestyle is one of the most effective methods to prevent accelerated ageing.[2] However, with the fast pace of modern life, it can be challenging to regulate one's lifestyle and dietary habits. The market offers numerous cosmetic products to combat skin ageing, but the role of synthetic ingredients used in the cosmetic products have apparent impact on human health and surrounding.[3]

Therefore, a potential strategy is to incorporate natural dietary supplements, functional foods, and nutraceutical agents that have been tested and deemed safe. Incorporation of such nutricosmetic or nutraceutical agents completes the "beauty from inside and beauty from outside" cycle of the body.[4]

Skin ageing due to extrinsic factors such as ultraviolet rays and subsequent oxidative insult can increase the imbalance between antioxidant defence system of the body and free radicals generated within. The balance can be restored by supplementing the skin through topical agents or nutraceutical agents including antioxidants, enzymes, or botanicals.[5] Literature suggests that antioxidant supplements can improve skin health viz., vitamins, beta carotene (6-15mg/day), biotin (30 mg/day), coenzyme Q (30-200 mg/day). Botanicals such as lutein, polyphenols (green tea polyphenols, EGCG, resveratrol), evening primrose, and pycogenol can also be consumed to prevent ageing.[6]

As mentioned earlier, botanicals have been reported throughout the history to prevent skin ageing but very few claims are supported by robust scientific and clinical evidences.[7] Amongst the many, polyphenols are botanicals of complex structures and used in cosmetics for their skin care benefits.[8] For instance, Flavagenol®, a polyphenol derived nutraceutical product, was given to 112 healthy women for 60 days by oral administration. The product improved clinical grades of photoaged skin along with reduced age spots.[9] Another botanical extract prepared from coffee silverskin is reported to have skin hydration benefits.[10] Green tea polyphenols administered topically and orally were also associated with reduction of skin ageing by increasing elastin tissue content, a property typical of polyphenols to inhibit MMP.[11] Matrix metalloproteinase II (MMP-2) is known to be involved in the progression of breakdown of collagen, elastin, and gelatine resulting in skin ageing.[12]

Similarly, a 35% polyphenol blend, CollaBZen™, developed by Zenherb Labs, is a product that combines three plant extracts: *Phyllanthus emblica*, *Camellia sinensis*, and *Coffea arabica*. This product was positioned as a collagen inducing blend of natural phytoconstituents. The product was proven beneficial in increasing 35% of collagen in human dermal fibroblast cells at a concentration of 0.05 mg/ml.[13] Current study emphasizes on the nutraceutical properties of CollaBZen™ blend containing capsules as an anti-ageing product. The authors assessed the action of the product on the human volunteers with moderate crow's feet wrinkles for skin firmness, skin elasticity, skin hydration, facial wrinkles, fine lines, skin texture, and skin tone evenness.

METHODS

The study protocol adopted was a 2-group, monocentric, randomized double blind, placebo-controlled study. The study protocol was reviewed and approved by independent ethics committee (Re-Registration number: ECR/245/Indt/MH/2015/RR-22) in C.L.A.I.M.S Pvt Ltd. The research study was carried out in accordance with the protocol, declaration of Helsinki, good clinical practice (GCP), and Indian council of medical research (ICMR) guidelines that pertain to medical research involving human subjects. Study skin parametric evaluations were made under the supervision of the principal investigator who was a trained dermatologist. The study was registered on CTRI (Clinical trial registry of India) on 04/10/2022. The registration number is CTRI/2022/10/046168. The study was scheduled from 09th November 2022 and ended on 04th February, 2023 and was conducted by C.L.A.I.M.S Pvt Ltd, Andheri, Mumbai, Maharashtra, India.

Placebo and CollabZen™

Hydroxypropyl methylcellulose (HPMC) capsules were used as a placebo control and labelled product A. The product B contained a blend of 250 mg of *Phyllanthus emblica*, *Camellia sinensis*, and *Coffea arabica* plant extract.

Subjects

A total of 64 volunteers participated in the study basis results of screening test. Men and women of age group 35-55 years were enrolled in the study and included those whose showed moderate crow's feet wrinkles, healthy skin in the test area, agreed to discontinue the use of any cosmetic products during the study, have no history of use of dietary supplements (collagen or vitamin C) and medicines 45 days prior to the start of the study, volunteers with no known allergies, and those who signed the informed consent. The volunteers were further instructed to have minimum exposure to UV during the study. Subjects involved in a different trial (1 month prior to the start date for current study), or with abnormal blood levels, any cutaneous conditions, severe acne, systemic diseases, gastric problems, allergies to product ingredients (gluten, wheat flour, eggs, and milk products), using any substances (alcohol, drugs), and pregnant women were not included in the study.

Protocol

Random allocation of products (A and B) was done. The placebo (n=32) group received product A, an identical labelled control, (Placebo capsules) and treatment group received (n=32) received product B (CollaBZen™ capsules). Both groups were instructed to take one capsule in the morning after breakfast and second capsule in the night after dinner for 8 weeks while maintaining a habitual lifestyle and eating habits. Clinical investigations were recorded by a medical doctor (Dermatologist) and a research assistant.

Primary evaluations including skin parametric assessments and questionnaire for efficacy were documented on day 0, week 4, and week 8. Secondary evaluation including questionnaire for tolerance were documented for day 0, week 4, and week 8. At the screening day and week 8, the routine blood investigations were done to ensure good health of the subjects (Figure 1).

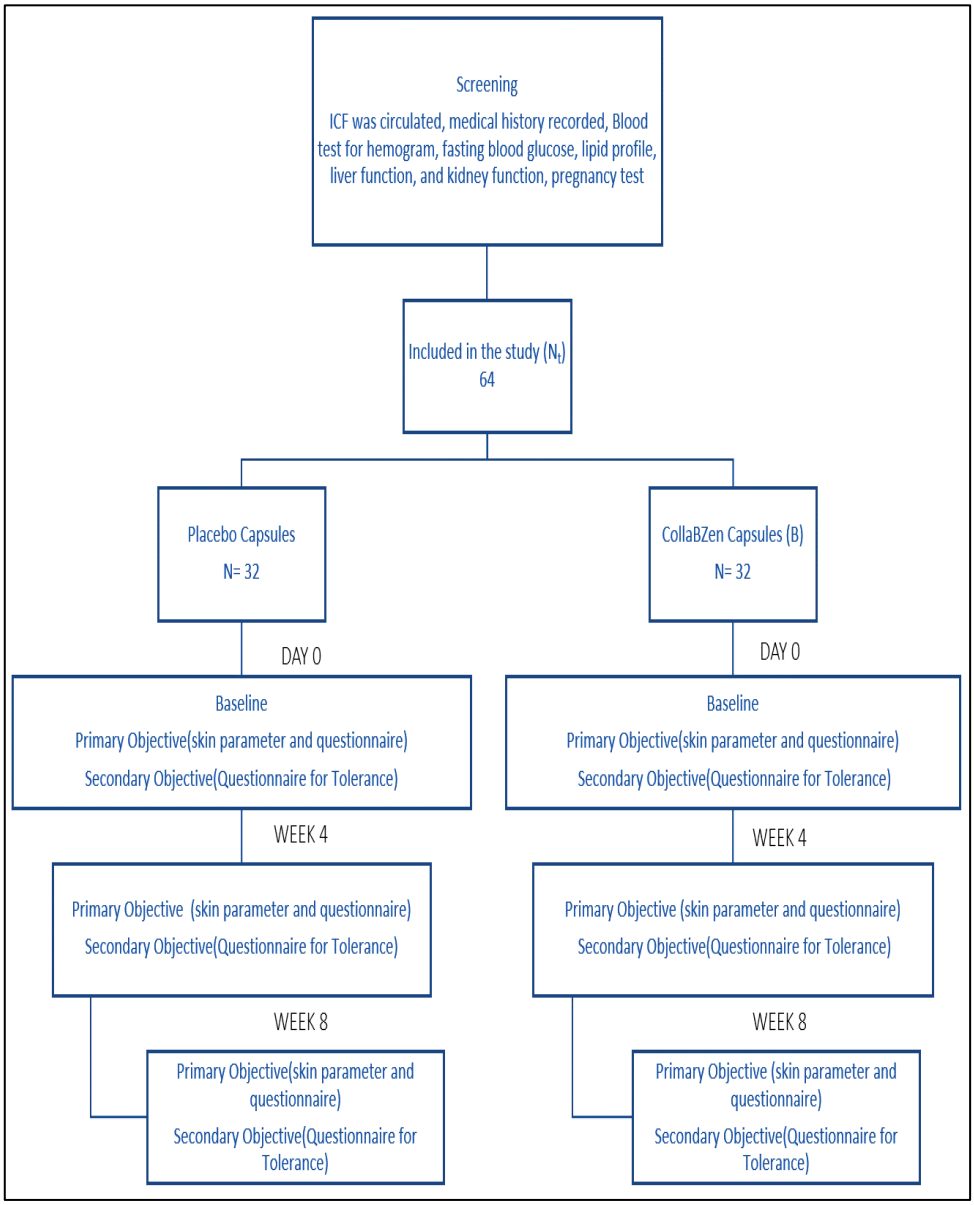


Figure 1: Flow chart of the study design.

Skin parametric evaluations

3D imaging using the optical 3D camera enabled the acquisition and analysis of skin images to evaluate facial wrinkles, fine lines, skin texture, and skin tone evenness. Photographs of the face/arms were taken while ensuring confidentiality. Skin firmness and elasticity was measured using a CutoMeter®. Skin hydration and deep skin hydration was measure by MoistureMeter SC and MositureMeter D respectively. A specific test site (2×3 cm) was identified on the participant's forearms for tape stripping. MositureMeter SC readings were taken during tape stripping using 15 tapes. Deep penetration and moisturization benefits were assessed after tape stripping at 0^{th}, 10^{th}, and 15^{th} strips. Transepidermal water loss (TEWL) measurements were recorded on VapoMeter. Furthermore, participants were requested to fill out a questionnaire to document their own observations of their skin health and tolerance towards the products at day 0, week 4, and week 8.

Statistical analysis

There were 2 drop outs in the study and the current study involves only 32 volunteers in each placebo and treatment group. Data was thus recorded for 64 volunteers. For every data point mean (or median) and standard deviation was calculated. Statistical analysis was carried out by 10.0 version of statistical software SPSS. Data was collected on day 0, week 4, and week 8. Dermatological parameters were tested for significant difference in means using Students t test. Subjective parameters were tested for significant difference in means using Chi Square analysis. The p values less than 0.05 were considered statistically significant.

RESULTS

Demographics of subject

The study included participants aged between 35.00 and 54.00 years (Table 1). The average age of group A was 45.00 years similar to the average age of group B (44.59 years). The difference in age between the two groups was not found to be statistically significant (p=0.737). The difference in gender between the two groups was also insignificant (p=0.605).

Table 1: Demographics of the subjects.

Parameters	Group A, (n=32)	Group B, (n=32)
Age (in years)		
Mean	45	44.59
SD	5.02	4.72
Range	36.00-54.00	35.00-54.00
Gender (%)		
Male	11 (34.4)	13 (40.6)
Female	21 (65.6)	19 (59.4)

Skin parametric evaluations

As seen in the Table 2, baseline parameters for the two groups, viz., treatment and placebo were not significantly different (p>0.05) except for mean skin hydration on face measured using MoistureMeter SC (p=0.022).

After 4 weeks, there was a significant reduction in mean wrinkle length (p=0.001) for the treatment group. However, the comparison of means for four weeks between treatment and placebo group did not exhibit any significant difference (p=0.143). At 8 weeks, both placebo and treatment groups exhibited significant reduction in mean wrinkle length in comparison to the baseline (p<0.02), but no significant difference was observed between the two groups (p=0.732). At week 4, there was no significant reduction in wrinkle depth observed for both treatment as well as placebo group in comparison to baseline groups respectively. However, on 8th week, statistically significant reduction in mean wrinkle depth was observed between baseline readings and 8th week reading for treatment group (p=0.001. There was a significant change in the mean skin tone evenness observed in the treatment group on both week 4 (p=0.002) and week 8 (p=0.008) assessment as compared to the baseline and improvement in skin tone evenness for placebo group was observed for week 4 (p=0.041) and not on week 8 (p=0.008). No difference between placebo and treatment group was observed (p>0.05).

There was a significant decrease in skin hydration (face, forearms after tape stripping it 10 times, and forearms after tape stripping it 15 times) found for the placebo group (p<0.02) as compared to the treatment group (p>0.05). The treatment group showed significant increase in skin hydration measured using MositureMeter D at the end of 8th week as compared to the placebo (0.009) which showed a time-dependent decrease in skin hydration (Figure 2). There was a significant increase in skin firmness R0 observed at both the weeks for the treatment group (p<0.02) as compared to baseline and placebo group. Contrary to this, the R0 increased significantly for placebo group indicating decreased skin firmness for both the weeks (Figure 3). As seen the Figure 4, there was a significant increase in elasticity of skin (Figure 5) of the subjects in the treatment groups observed as 8th week as compared to the baseline and placebo group (p<0.02).

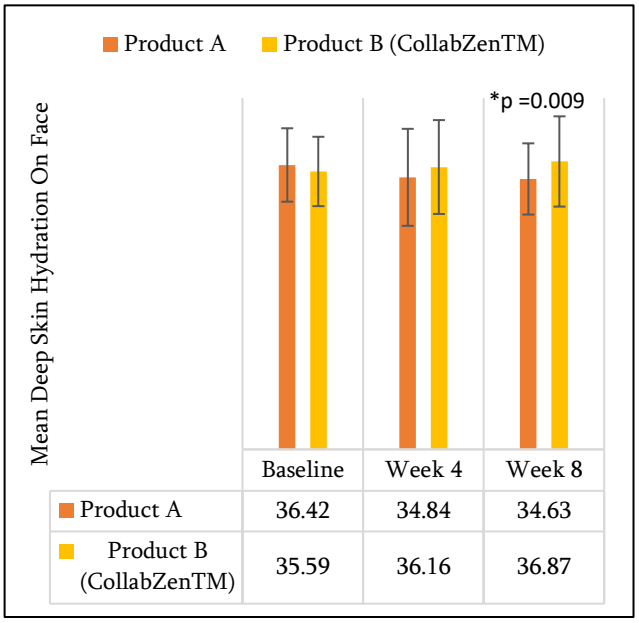


Figure 2: Skin hydration on MoistureMeter D at baseline, week 4, and week 8.
Note: p<0.05 is considered statistically significant.

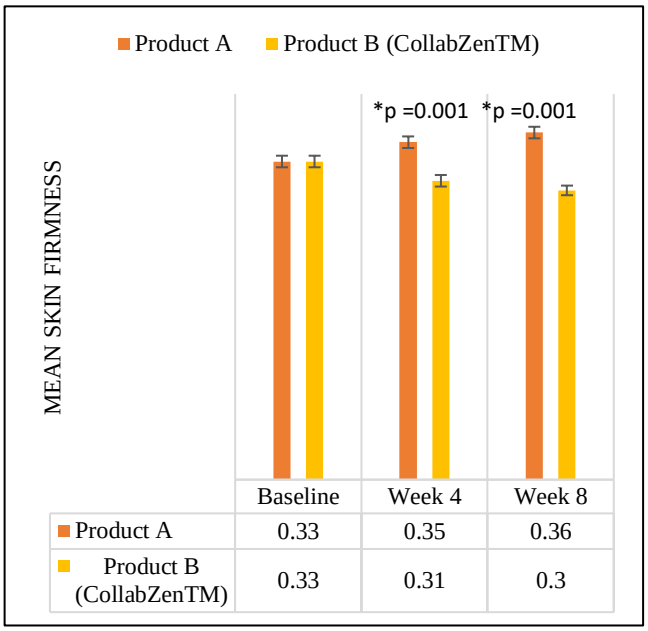


Figure 3: Skin firmness at baseline, week 4 and 8.
Note: p<0.05 is considered statistically significant.

Table 2: Primary evaluation using skin parameters as primary objective of the study.

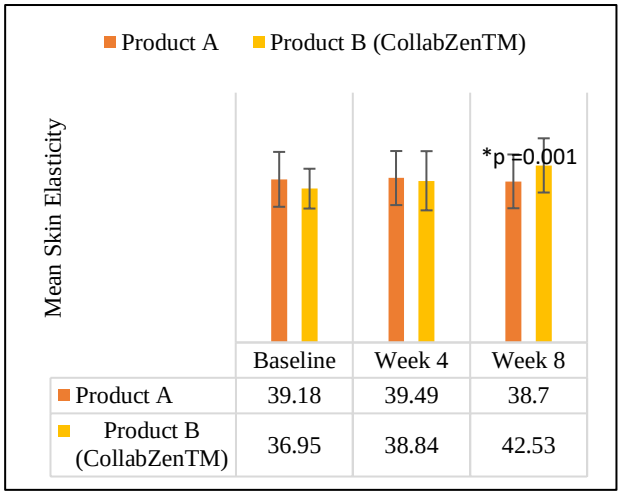
Skin parameters	Placebo			P1	P2	Treatment			P3	P4	P5	P6	P7
	Baseline	Week 4	Week 8			Baseline	Week 4	Week 8					
Mean wrinkle length	15.81±5.82	14.37±5.63	12.39±5.19	0.067	0.001	15.89±5.54	12.99±6.25	12.12±5.37	0.001	0.001	0.955	0.143	0.732
Mean wrinkle depth	0.043±0.005	0.043±0.005	0.043±0.006	0.167	1.000	0.043±0.006	0.042±0.006	0.041±0.007	0.068	0.001	1.000	0.027	0.096
Mean fine lines	9.09±2.89	8.72±2.80	9.41±2.89	0.455	0.522	8.78±2.51	9.19±3.49	8.81±3.13	0.405	0.948	0.648	0.262	0.673
Mean skin tone evenness	5.65±2.94	5.18±2.93	5.15±3.04	0.041	0.065	5.32±2.09	4.68±2.42	4.70±2.44	0.002	0.008	0.606	0.567	0.707
Mean texture roughness	0.150±0.050	0.149±0.046	0.142±0.043	1.000	0.138	0.145±0.046	0.139±0.041	0.148±0.064	0.228	0.575	0.678	0.447	0.197
Mean skin hydration on face	40.64±15.17	39.91±16.27	34.84±14.73	0.605	0.011	32.22±13.55	34.65±12.75	31.55±12.72	0.080	0.739	0.022	0.108	0.086
Mean deep skin hydration on the forearm (ten strips)	39.35±10.49	38.71±09.19	34.38±08.34	0.466	0.001	38.27±14.53	37.25±12.05	35.86±11.01	0.540	0.209	0.734	0.839	0.276
Mean deep skin hydration on the forearm (fifteen strips)	45.10±12.77	44.55±12.46	41.64±10.23	0.516	0.013	44.69±15.00	44.92±13.72	44.51±13.00	0.882	0.93	0.906	0.657	0.183
Mean deep skin hydration on face	36.42±4.70	34.84±6.21	34.63±4.56	0.217	0.071	35.59±4.44	36.16±6.01	36.87±5.78	0.508	0.047	0.470	0.161	0.009
Mean skin firmness	0.33±0.06	0.35±0.06	0.36±0.06	0.008	0.001	0.33±0.06	0.31±0.06	0.30±0.05	0.001	0.001	1.000	0.001	0.001
Mean skin elasticity	39.18±6.59	39.49±6.49	38.70±6.46	0.694	0.636	36.95±4.78	38.84±7.11	42.53±6.51	0.165	0.001	0.126	0.309	0.001
Mean TEWL	31.92±10.28	32.11±09.78	33.36±09.46	0.840	0.234	30.33±10.66	30.67±09.76	30.90±10.34	0.611	0.414	0.545	0.896	0.535

Note: The values are expressed as average ± SD. P1-Comparison of means between baseline and week 4 for placebo group (Product A). P2-Comparison of means between baseline and week 8 for product A. P3-Comparison of means between baseline and week 4 for treatment group (Product B). P4-Comparison of means between baseline and week 8 for product B. P5-Comparison of means for baseline between product A and product B. P6-Comparison of means for week 4 between product A and product B. P7-Comparison of means for week 8 between product A and product B. p value (Students t test analysed) above 0.05 is considered statistically significant and are highlighted in grey.

Table 3: Primary evaluation using questionnaire as primary objective of the study.

Parameters	Group A		Group B		P1	P2
	Week 4	Week 8	Week 4	Week 8		
Reduced wrinkles	18.8	0.0	34.4	59.4	0.157	0.001
Reduced fine lines	28.1	21.9	53.1	62.5	0.041	0.001
Hydration	59.4	28.1	56.3	62.5	0.800	0.005
Smooth and soft skin	56.2	28.1	75.0	65.6	0.114	0.002
Firm and tight skin	40.6	15.6	56.2	53.1	0.211	0.001
Even skin appearance	50.0	12.5	50.0	90.6	1.000	0.001
Overall improvement	40.6	12.5	56.2	90.6	0.211	0.001
Overall product was good	53.1	12.5	75.0	81.2	0.068	0.001

Note: The values are expressed as average ± SD. P1-Comparison of means between product A and B for week 4. P2-Comparison of means between product A and B for week 8. P value (Chi square analysed) above 0.05 is considered statistically significant and are and are highlighted in grey.



	Baseline	Week 4	Week 8
Product A	39.18	39.49	38.7
Product B (CollabZenTM)	36.95	38.84	42.53

Figure 4: Skin elasticity at baseline, week 4 and 8.
Note: $p<0.05$ is considered statistically significant.

Figure 5: Effect of product B on improving the skin elasticity in both male and female volunteers.

Subjective assessments

A significantly higher proportion of participants who consumed product B, CollaBZen™ capsules, reported positive outcomes compared to those who consumed placebo (Table 3). Specifically, 59.4% acknowledged reduction in wrinkles, 62.5% observed a decrease in fine lines and 62.5% experienced improved facial skin hydration. Additionally, 65.6% noted that their facial skin became soft and smooth, while 53.1% reported it became firm and tight. Furthermore, 90.6% of participants noticed enhancement in facial skin tone evenness and overall appearance. In terms of overall satisfaction, 81.2% of participants expressed a preference for test product B, CollaBZen™ capsules. At week 8, treatment group demonstrated higher levels of satisfaction in all aspects related to their perceived skin health.

DISCUSSION

Environmental factors and natural programmed ageing can alter the levels of collagen in our body by either increased production of matrix metalloproteinase (MMPs) or affecting the ability of skin to produce more collagen as the fibroblasts age.[14] It is thus crucial to optimize the collagen levels by either taking collagen supplements or using compounds that can boost collagen levels.[7]

Our previous study has proven the collagen-promoting ability of CollabZen™ in human dermal fibroblast cells.[13] The product CollabZen™ contains a blend prepared from three different plant materials viz., *Phyllanthus emblica*, *Camellia sinensis*, and *Coffea arabica.* The same product in form of capsules was formulated and was tested for its anti-ageing ability as a nutraceutical agent on actual human volunteers.

The potential use of this collagen promoting nutraceutical product was subjected testing its effect on skin ageing with respect to reduction in fine lines, wrinkles, uneven skin tone, and skin hydration. The current study compared a treatment product (CollaBZen™ containing tablets) and placebo for their effects on skin ageing in human volunteers for 8 weeks. The treatment group showed a significant reduction in improved skin hydration by 6.46%, firmness by 20%, and elasticity by 9.89% by the end of 8 weeks.

In the cosmetic industry, green tea extract works as an antioxidant agent counteracting the harmful effects of ultraviolet rays and exhibit anti-ageing benefits.[15] The tea polyphenols are strong scavenger of free radicals and has DNA-damage inhibitory properties.[16] Recently, a cosmeceutical bioextract constituting probiotics along with *Camilla sinensis* extract was also proven to show anti-MMP and anti-tyrosinase activity.[17] Several formats of green tea extracts are being studied to discover its potential in cosmetic, pharmaceutical, and nutraceutical sector. Literature is present on the skin health improving ability of *Camilla sinensis* as a nutraceutical product tested in human volunteers. In a double-blind placebo-controlled study, volunteer either consumed a green tea polyphenol beverage or a control beverage. At the end of a 12-week trial, it was found that polyphenol enriched beverage protected the skin from UV-damaged generated via solar simulator and improved the quality of the skin of the women.[18] A Yuliv™ collagen drink containing green tea extract enriched with vitamin C (800 mg) is a nutraceutical product available in market in the skin care sector and has been recently proven to improve skin, hair, and heart health.[19] Several reports exist on the effect of *Camilla sinensis* nutraceutical products in human volunteer to combat signs of ageing, acne, and UV-induced skin damage.[20]

There are several reports suggesting the utilization of *Phyllanthus emblica* in nutraceutical sector by virtue of its pharmacological activities apart from the strong antioxidant potential.[21] These pharmacological activities such as cardioprotective, anti-diabetic, and anticancer property can be attributed to the presence of phytochemicals such as polyphenols, gallic acid, quercetin, emblicalin A, and emblicalin B.[21] It is also a popular ingredient used in the cosmetology sector.[13] The anti-ageing effects of amla fruit was also assessed *invitro* by Pientaweeratch et al and amla showed the highest polyphenol content and moderate anti-collagenase ability.[23] The effects of an oral supplement containing *Phyllanthus emblica* fruit extract along with vitamin E and carotenoids was evaluated in vitiligo patients for 6 months and the blend showed signs re-pigmentation in treated patients.[24]

Coffee pulp extract formulated as a face serum and a coffee pulp drink was investigated for anti-ageing potential *invitro* and in human volunteers. The volunteers consuming coffee pulp drink exhibited better skin health in terms of skin moisture, brightness, and collagen density. Thus, proving the delay in ageing effects of coffee extract in nutraceutical segment.[25]

Over the years, the botanicals extracted from amla, green tea, and coffee are implemented in skin care regimen protecting the skin from harmful effects on chronological and accelerated ageing. However, the combination of these potent polyphenol rich plant materials in CollaBZen^{TM}, until now, were not investigated for its potential to enhance collagen production *invitro* and combat signs of ageing in human volunteers.[25] As a result, this product has the potential to revolutionize the cosmetic industry by introducing groundbreaking anti-ageing properties through nutraceutical intervention.

Limitations

The study was limited to only the healthy participants. The effect of CollabZen^{TM} as a nutraceutical agent on photodamaged, acne-prone, or affected skin was not undertaken as a part of the study. The study was conducted only for 8 weeks and assessment of long-term effects of the product is required. The participants were not instructed to maintain a constant diet and this may further affect the efficacy of the nutraceutical product under study.

CONCLUSION

With the growing interest in nutraceuticals and natural solutions for skincare, CollaBZen^{TM} has the potential to fill a significant gap in the market. The product's innovative approach, supported by scientific research, sets it apart from existing nutraceuticals. Its collagen-promoting and anti-aging properties make it a compelling choice for consumers seeking effective and natural solutions for maintaining youthful skin. In conclusion, CollaBZen^{TM} presents a promising opportunity for market entry and potential success in the skincare industry. Further research, marketing efforts, and endorsements from skincare experts could help establish CollaBZen^{TM} as a leading nutraceutical product, catering to the growing demand for natural and effective anti-aging solutions.

ACKNOWLEDGEMENTS

Author would like to thanks to C.L.A.M.S. PVT LTD and Zywie Ventures Pvt. Ltd. for their expertise towards the conceptualization and conduct of the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Gadani MC, Badak S, Upadhyay R. Anti-ageing effects of CollabZen™ in healthy human volunteers: a randomized, double blind, placebo-controlled study. Int J Clin Trials 2024;11(2):109-16.