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Cosmeceutical Synbiotic

A multifunctional Synbiotic Ingredient for Topical
and Oral Applications

Safety, Stability and Proof of Efficacy



Bio-az Cosmeceutical Synbiotic Elements

Bio-az Cosmeceutical Synbiotic is a synergistic blend crafted to complement and enhance each individual element, offering a unique contribution for gut and cutaneous health.

Pre-Prep Catalyst: Terminalia Chebula

Accredited in Ayurvedic medicine, it is known as 'The King', boosting a plethora of beneficial bio-active compounds.

Probiotic: Bacillus subtilis

Plays a fundamental role in the induction, training and function of the host metabolism, immunity and response to infection. Identified with over 24 distinct natural antibiotics.

Postbiotic: Lactobacillus Plantarum

Releases beneficial metabolites that have a profound effect on the gut-skin axis, that have been shown to upregulate production of hyaluronic acid and increase ceramide levels.

Prebiotic: Inulin

Sourced from Chicory Root, promotes the growth of beneficial bacteria and helps them to thrive, strengthening the skin barrier.



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Safety, Stability and Proof of Efficacy

Case Study: 26-year-old female

Symptoms:

- Painful to touch facial skin so could never touch her face.
- Sebaceous secretion, rosacea, acne and lesions covering entire facial region. Redness, swelling.
- Diagnosed with Ulcerative Colitis.

Length of time symptoms have been present: Infancy.

Preparation: 4% of Bio-az Cosmeceutical Synbiotic and mixed into 500 grams of natural base cream.

Course of treatment:

Application: Twice daily.

Results after 2 hours: Within two hours of the first application, the participant experienced heat in the facial region (immune system stimulated). The symptoms began to dissipate.

Within 48 hours the inflammation was reduced to where the girl could touch her face.

Pain was completely gone within 48 hours.

Tightness underneath her chin became more flexible.

Redness and swelling were completely gone.

Acne rosacea lesions continued to dissipate.



Day 1 before application



Day 4 of twice-daily application

Case Study: 17-year-old male

Symptoms:

- Suffering from cystic acne.

Topical Preparation: A formulation containing natural ingredients and Bio-az Cosmeceutical Synbiotic was applied twice per day, morning and evening.

Results: After 3 days of use, inflammation was reduced, redness and swelling were reduced and lesions began to diminish.



Before



Before



After 3 days



After 3 days

Case Study: 45-year-old Polynesian/Scottish male

Symptoms:

- Suffering from symptoms of psoriasis for 23 years

Topical Preparation: Natural base cream was prepared with 4% Bio-az Cosmeceutical Synbiotic.

Application: The cream was applied twice per day for 7 days and then for a further 14 days twice per week.

Results: After 7 days the symptoms were reduced where there was no irritation, no itching, no redness and the skin began to repair. The participant continued to use the cream twice only per week and the results were maintained.



Before



Before



After 7 days



After 7 days

Safety, Stability and Proof of Efficacy

Bio-az® Cosmeceutical is a unique synbiotic ingredient that can be used as a functional ingredient in a variety of skincare applications due to its high stability and tolerance to acid, salt and temperature.

Stability

Shelf Life: 24 months

Physical and chemical properties:

Density: 0.45-0.6 g/mL*

Particle Size: Max 600 µm

Solubility: Soluble in water

Form: Powder

Appearance: Beige to pale yellow

Odour: Slightly sweet odour

Taste: Slightly sweet

Moisture: Max 5%

Efficacy

Bio-az Cosmeceutical Synbiotic Elements

The Bio-az Blend synergises the catalytic capabilities of Terminalia Chebula, the probiotic attributes of Bacillus subtilis, the bioactive benefits of postbiotic Lactobacillus plantarum, and the nourishing properties of Inulin from Chicory root, offering a ground-breaking approach to skincare through microbiome optimisation.

Terminalia Chebula (TC) - Pre-prep catalyst

In pursuit of sustainability, Bio-az's Chief Scientific Officer collaborated with rural Indian farming communities to establish an ecologically responsible approach to herbal extraction of Terminalia Chebula at their GMP-certified facility. Traditional TC fruit underwent rigorous evaluation, exploring various solvents including water, ethanol, methanol, and HCl, resulting in higher concentrations of active compounds.

This established the process for standardisation of Terminalia Chebula yielding chebulinic and chebulagic compounds, achieved through a comprehensive methodology.



Pre-prep catalyst Study 1

Terminalia Chebula (TC) extract sustains long-lasting antioxidant capacity when irradiated with UVR that simulates daylight conditions **for 4 consecutive hours in contrast with a solution of α -Tocopherol** whose antioxidant capacity degraded rapidly within the first hour of exposure.

Randhawa et al

Dovepress

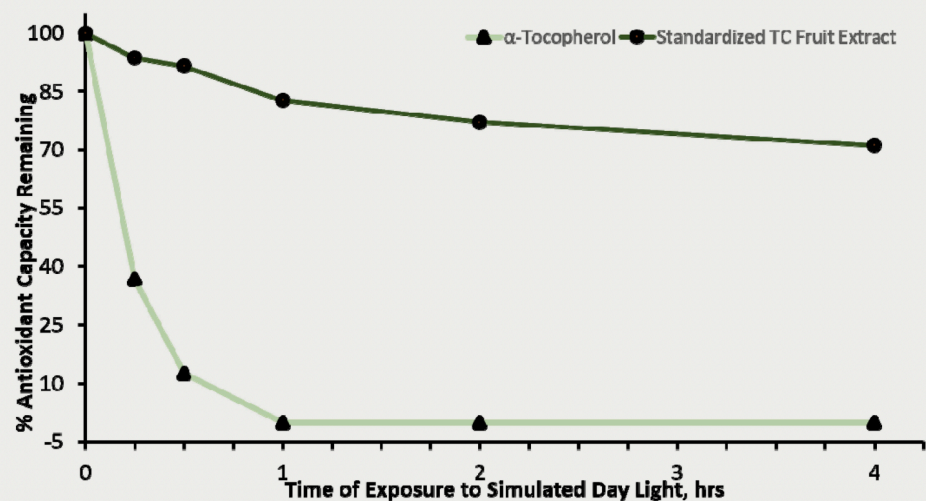


Figure 1 A solution of standardized TC fruit extract sustains long-lasting antioxidant capacity when irradiated with UVR that simulates day light conditions for 4 consecutive hours in contrast with a solution of α -tocopherol whose antioxidant capacity degraded rapidly within the first hour of exposure.

← **TC**
Antioxidant capacity 4 consecutive hours.

← **α -Tocopherol**
Antioxidant capacity degraded within the first hour.

Pre-prep catalyst Study 2

TC cutaneous wound healing – Antibacterial activity

Tannin extracts of TC effectively prevent the invasion of foreign microbes, avoiding enlargement and the development of an infected wound.

Normal bacterium shows a smooth surface, plump appearance and good refraction.

- At 24 hours after treatment, the majority of the bacteria of the group shrank and became dry and distorted.
- Changes showed that tannin extracts destroyed pathogenic bacteria including *Staphylococcus aureus* and *Klebsiella pneumoniae*.

Study 2 reference:

Kun Li, Yunpeng Diao, Houli Zhang, Shouyu Wang, Zhen Zhang, Bo YU, Shanshan Huang, Hong Yang. Tannin extracts from immature fruits of *Terminalia chebula* Fructus Retz. Promote cutaneous wound healing in rats. *BMC Complementary and Alternative Medicine* 2011, 11:86. <http://www.biomedcentral.com/1472-6882/11/86>

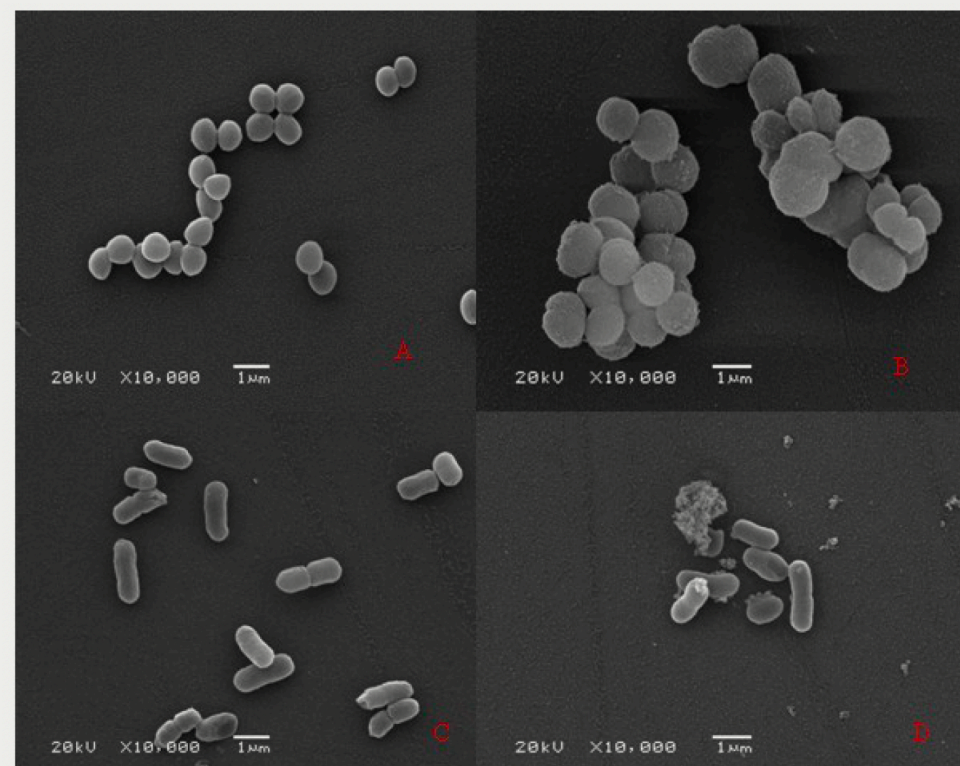


Figure 2 Morphology of *Staphylococcus aureus* and *Klebsiella Pneumonia* under scanning electron microscope. A the normal morphology of *Staphylococcus aureus*; B the morphology of *Staphylococcus aureus* on 24 h; C the normal morphology of *Klebsiella Pneumonia*; D the morphology of *Klebsiella Pneumonia* on 24 h

Pre-prep catalyst Study 3

Anti-ageing - Elastase and Hyaluronidase Inhibitory Activity

Study 3 reference: Song-Ja Kim, Sandesh A. Sancheti, Shruti S. Sancheti, Byung-Hun Um, Seon-Mi Yu, Sung-Yum Seo, Effect of 1,2,3,4,6-penta-O-galloyl-beta-D-glucose on elastase and hyaluronidase activities and its type II collagen expression. Acta Poloniae Pharmaceutica – Drug Research, Vol. 67, No. 2, pp. 145-150, 2010. ISSN 0001-6837, 23 September 2009.

80% Elastase Inhibitory activity

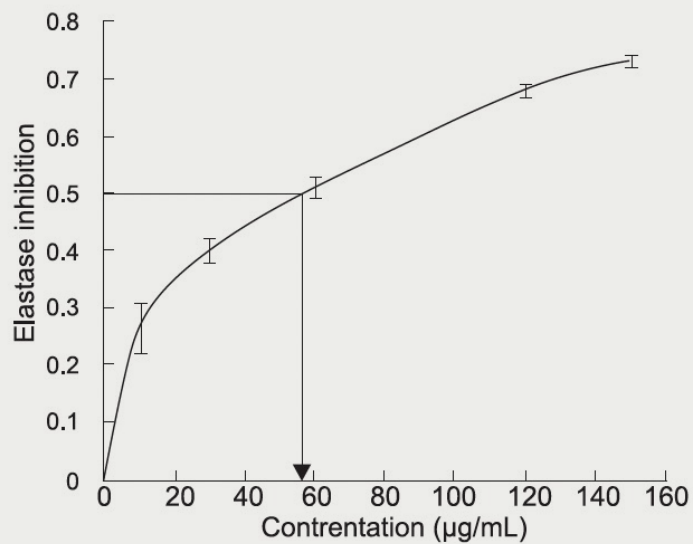


Figure 2. Elastase inhibitory activity of compound 1

87% Hyaluronidase inhibitory activity

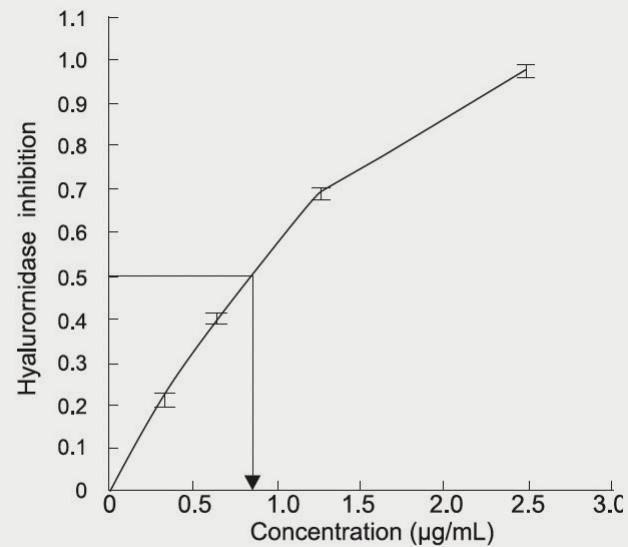


Figure 3. Hyaluronidase inhibitory activity of compound 1

Bacillus subtilis (B. subtilis)

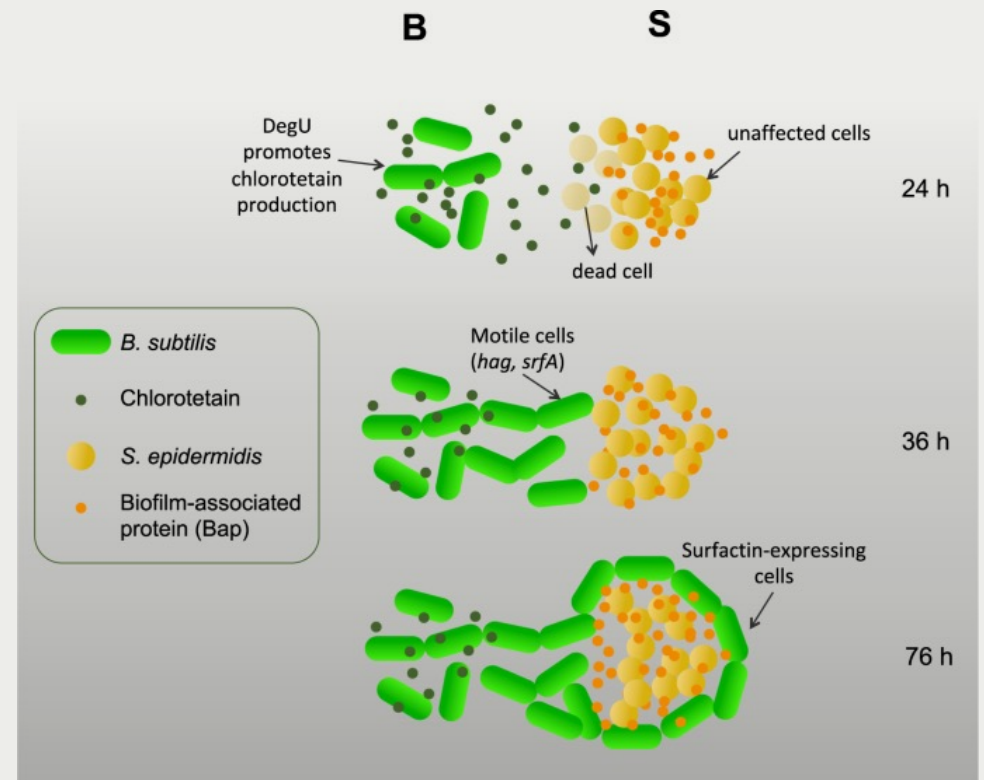
Probiotics are defined as “live microorganisms which, when administered in adequate amounts confer a health benefit to the host”. A live probiotic will display a live colony-forming count (CFU) that can be measured. *B. subtilis* is well-suited as a probiotic and is recognised for its therapeutic benefits.

- *B. subtilis* is extremely resistant to all manner of environmental extremes. It is highly resistant to heat and desiccation. It is stable over a wide range of pH levels.
- *B. subtilis* is non-pathogenic to humans and naturally found on human skin.
- *B. subtilis* is considered a safe probiotic by WHO/FAO and the ISAPP.
- *B. subtilis* incorporation finds relevance across a range of applications.

Bacillus subtilis Study 4

***B. subtilis* engulfs pathogenic *S. epidermidis* in three stages:** (a) quorum sensing, (b) sliding motility to reach *S. epidermidis*, and (c) surrounding the *S. epidermidis* colony and engulfing it.

Study 4 reference: Jhonatan A. Hernandez-Valdes, Lu Zhou, Marcel P. de Vries, Oscar P. Kuipers. Impact of spatial proximity on territoriality among human skin bacteria.



Bacillus subtilis Study 5

Bacillus subtilis natto – Activation effects on *S. aureus* and *C. albicans*.

Study 5 reference: Japan Natto Kinase Association. http://j-nattokinase.org/en/jnka_nattou_02.html

Growth stunting function against *S. aureus*

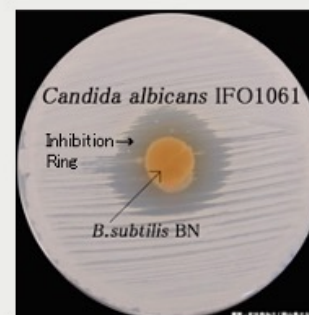
Activation effect of *Bacillus subtilis* natto against *Staphylococcus aureus* (*S. aureus*)



Bacillus subtilis natto cultured agar was punched out and placed on an *S. aureus* smeared plate. As the result, an inhibition ring was created around the agar.

This means ***Bacillus subtilis* natto** has a growth stunting function against *S. aureus*.

Activation effect of *Bacillus subtilis* natto against *Candida albicans* (*C. albicans*)



Bacillus subtilis natto cultured agar was punched out and placed on a *C. albicans* smeared plate. As the result, an inhibition ring was created around the agar.

This means ***Bacillus subtilis* natto** has a growth stunting function against *C. albicans*.

Bacillus subtilis Study 6

Natural antibiotics

B. subtilis the model system for Gram-positive organisms is able to produce more than two dozen antibiotics with an amazing variety of structures.

Identified antibiotics produced by *Bacillus subtilis*:

Bacitracin, Subtilin, Ericin S, Ericin A, Mersacidin, Sublacin, Subtilosin A, turin, Bacilomycin, Mycosubtilin, Fengycin Plipastatin, Bacilysin, Bacilysocin, Amicoumacin, Surfactin

Study 6 reference: T. Stein. Bacillus subtilis antibiotics: structures, syntheses and specific functions. DOI: 10.1111/j.1365-2958.2005.04587.x

Clinical study – *B. subtilis* – application Study 7

Polyvinyl alcohol microparticles

The research revealed that wounds treated with PVA microparticles healed in 12 days, quicker than the untreated group (15 days). No skin irritation or infection emerged during a 15-day postoperative period.

This study indicates that live bacterial formulations could yield continuous antimicrobial agents, restraining pathogenic bacteria.

Study 7 reference: Bacillus subtilis - applications – Wound Healing in Polyvinyl alcohol microparticles Ben David, N., et al. Bacillus subtilis in polyvinyl alcohol (PVA) microparticles for treating open wounds. Ben David, N., Mafi, M., Nyska, A., Gross, A., Greiner, A., Mizrahi, B. Bacillus subtilis in PVA Microparticles for Treating Open Wounds 9 September 2022. ACS OMEGA <http://doi.org/10.1021/acsomega.1c00790>

Bacillus subtilis Study 8

B. subtilis strains enhance tyrosinase inhibitory activity.

B. subtilis strains boost tyrosinase inhibitory activity, primarily through prolific arbutin production. This results in skin-lightening effects and potential anti-neurodegenerative benefits.

Arbutin, a potent tyrosinase inhibitor and antioxidant, is notably produced.

Compared to reference strains like B. licheniformis, B. coagulans, and B. pumilus, B. subtilis strains in the study demonstrated significantly higher arbutin levels.

Arbutin's precursor is hydroquinone, which in turn originates from polyphenols. Bacillus subtilis natto is rich in polyphenols, serving as arbutin precursors during fermentation.

Study 8 reference: Hun Jin, Y., Jeon, A.R., Mah, J. Tyrosinase Inhibitory Activity of Soybeans Fermented with Bacillus subtilis; Capable of Producing a Phenolic Glycoside, Arbutin. National Library of Medicine; PubMed, 18 Dec 2020; <https://doi.org/10.3390/antiox9121301>

Bacillus subtilis Study 9

Bacillus subtilis heals keratinocytes after sodium arsenite (SA) injury.

(Petruk et al., 2018)

In the presence of sodium arsenite oxidative stress, this study examined the impact of B. subtilis spores on human keratinocytes.

The study revealed that B. subtilis spores emerge as a potential agent to counteract oxidative stress in human keratinocytes.

Study 9 reference: Petruk, G., Donadio, G., Lanzilli, M., Isticato, R., Monti, D.M. Alternative use of Bacillus subtilis spores: protection against environmental oxidative stress in human normal keratinocytes. Scientific Reports 29 January 2018; <https://doi.org/10.1038/s41598-018-20153-2>

Postbiotic – Lactobacillus plantarum Oral application Study 10

Skin Hydration

- Enhances HA production by upregulating HA production contributing to the moisture content and barrier function of the skin.
- Prevention of UV-induced transepidermal water loss (TEWL) .
- Antimicrobial effects.
- Anti-photoageing effects through reduction of wrinkle formation and suppression of epidermal thickening and skin hydration increases in association with increasing ceramide levels.
- Promotes improvement of skin elasticity.
- <https://cdn.jwplayer.com/previews/t0UvPFV7>

Study 10 reference: Dong Eun Lee, Chul-Sung Huh, Jehyeon Ra, Il-Dong Choi, Ji-Woong Jeong, Sung-Hwan Kim, Ja Hyun Ryu, Young Kyoung Seo, Jae Sook Koh, Jung-Hee Lee, Jae-Hun Sim, and Young-Tae Ahn. Clinical Evidence of Effects of Lactobacillus plantarum HY7714 on Skin Aging: A Randomised, Double Blind, Placebo-Controlled Study. 2 October 2015. <http://dx.doi.org/10.4014/jmb.1509.09021>.

Postbiotic – Lactobacillus plantarum Study 11

Topical application of Lactobacillus plantarum on severe human burns has been described to improve tissue repair and prevent infection (Peral et al. 2009).

L. plantarum shows high and comprehensive potential as an agent to modify dermal properties and skin health when applied topically.

Heat-killed Lactobacillus spp., including both water-soluble and water-insoluble components, is able to improve skin health.

Patent – International Publication Number WO 2020/002429 A1.

Study 11 reference: Maria C. Peral, Miguel A. Huaman Martinez, Juan C. Valdez. Bacteriotherapy with Lactobacillus plantarum in burns. DOI: 10.1111/j.1742-481X.2008.00577.x

Inulin – sourced from Chicory Root

Fosters the growth of beneficial bacteria, bolstering the skin barrier and enhancing the proliferation of good microorganisms.

- Decreases harmful bacteria in favour of naturally occurring friendly microorganisms on the skin.
 - Acts as a natural humectant, drawing moisture from the environment into the skin to maintain hydration.
 - Counteracts elements contributing to redness, dryness, and ageing.
 - Exhibits antioxidant properties.
 - Displays anti-inflammatory effects.
 - Gentleness assured, avoiding irritation.
-

Inulin reference: Zofia Nizioł-Lukaszewska, Tomasz Bujak, Tomasz Wasilewski, Edyta Szmuc. Inulin as an effectiveness and safe ingredient in cosmetics.

The background of the image features three translucent, rose-gold spheres of varying sizes. Each sphere contains a detailed molecular model, likely representing a protein or a complex organic molecule. The spheres are resting on a surface that appears to be a crystalline or molecular lattice, also rendered in a translucent, rose-gold style. The lighting is soft and diffused, creating a warm, ethereal atmosphere. The overall composition suggests a focus on molecular biology, chemistry, or nanotechnology.

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