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Controlling Alzheimer's and Degenerative Diseases with Stem Cells Stimulated by Fortified Mangosteen Extract

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ABSTRACT

Alzheimer's Disease (AD) remains a critical neurodegenerative challenge. This study evaluates BIM AD®, an improved formulation containing Fortified Mangosteen Extract, for its potential in preventing and slowing AD progression. We assessed stem cell markers, inflammatory cytokines, autophagy-related genes, telomere length, gene expression changes, T cells, and AD-related biomarkers in participants at baseline and at follow-up intervals of weeks 4 and 8. Supplementation with BIM AD® at 6 capsules/day in 8 participants for 8 weeks significantly increased the expression of stem cell-associated markers, stemness-related transcription factors, and CD34 counts. Immunological analysis revealed a significant decrease in pro-inflammatory cytokines (interleukin-17A [IL-17A] and TNF-α), alongside increased levels of FOXP3 and IL-10, and enhanced natural killer T cell activity, indicated by elevated IFN-γ. Furthermore, the formulation stimulated cellular recycling through autophagy-related genes, leading to telomere lengthening via new stem cell stimulation, and significantly reduced AD-specific pathology, notably p-tau 217 and the p-tau 181/t tau ratio. In conclusion, BIM AD® is beneficial for remedying AD, as well as inflammation and degeneration in all systems of the body.

Keywords

Age reversal, Alzheimer's disease (AD), Autophagy, BIM AD®, Black sesame seeds, Cytokines, Degenerative diseases, Fortified Mangosteen Extract, Gene expression, Guava fruit, Mangosteen aril, Pennywort leaves, P-tau, Soybeans, Stem cells, T cells, Telomeres.

Background

We have previously published an article on Regenerative Innovation from Fortified Mangosteen Extract [1], which investigated alterations in T cells, cytokines, telomeres, and autophagy in 19 participants, and concluded that the formulation has the potential to prevent Alzheimer's Disease (AD). We are now reporting an improved formulation, which shows a definite effect in preventing and slowing AD progression. The product is registered with the Thai FDA as BIM AD®.

Materials and Methods

Preparation of BIM AD®

The dietary supplement Fortified Mangosteen Extract, BIM AD®, is formulated based on Mylife®/Mylife100®, but with a different concentration of active ingredients derived from five edible plants, namely pennywort leaves, black sesame seeds, soybeans, guava fruit, and mangosteen aril. Mangosteen aril juice powder is prepared by grinding, centrifuging, filtering, and spray-drying the juice. Pennywort leaf powder is obtained by heating and centrifuging an extract from the dried leaves. Guava juice powder is produced by grinding, filtering, and spray-drying the juice, while black sesame and isolated soybean protein powders are processed similarly through grinding, centrifuging, and drying steps. Each capsule contains specific doses of these powders [2].

Subjects

The study included 8 participants (7 females and 1 male) with an age range of 60 to 86 years. All participants were generally healthy, non-drinkers, non-smokers, and had no chronic illnesses requiring regular medication.

Study Design

The study spanned 8 weeks, with each participant attending three scheduled visits: at week 0 (first visit), week 4 (second visit), and week 8 (third visit). During weeks 1-8, 3 capsules of BIM AD® were taken before breakfast and 3 capsules before dinner. Body composition data and blood samples were collected at each visit. Participants were instructed to maintain their usual lifestyle, including their daily dietary intake and exercise habits, throughout the entire 8-week period.

Blood Sample Collection and Parameters Analyzed

Blood samples were collected by venipuncture after a 12-hour fasting period to measure various biomarkers using an automated blood BS-400 chemistry analyzer for hemoglobin, fasting plasma glucose, blood urea nitrogen (BUN), creatinine, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamate pyruvate transaminase (SGPT). An aliquot of EDTA blood was obtained to assess complete blood counts, cytokines, autophagy gene expression, p-tau 217 (phosphorylated tau 217), p-tau 181/t tau, Aβ42/Aβ40 (amyloid β), stem cell-associated gene expression, telomere length, and CD4, CD8, and CD34 cell counts.

Measurement of Body Composition

Body weight, height, body mass index (BMI: kg/m^2), body fat (% of body weight), fat mass (kg), fat-free mass (FFM: kg), muscle mass (kg), total body water (%), bone mass (kg), and visceral fat were measured using a Tanita BC-420MA body composition analyzer (Tanita Corporation, Tokyo, Japan) [2].

Measurement of Cytokines and P-Tau 217

Using the enzyme-linked immunosorbent assay (ELISA) technique, the anti-inflammatory properties of the compounds isolated from human plasma were determined. Whole blood was separated into plasma using a K3EDTA vacuum tube. The human plasma samples were analyzed to determine the concentrations of human IL-6, IL-10, IL-17A, IFN-γ, TNF-α, and IL-12/IL-23 (p40) using the ELISA MAX™ Deluxe kit (BioLegend, USA), whereas FOXP3 (Forkhead box P3) and p-tau 217 were determined using an ELISA kit (Biorbyt, USA).

All ELISA assays were performed according to the manufacturer's instructions. For IL-6, IL-10, IL-17A, IFN-γ, and TNF-α, the standards were prepared at concentrations ranging from 0 to 500 pg/mL, whereas the IL-12/IL-23 (p40) standards were prepared at concentrations ranging from 0 to 2,000 pg/mL. The FOXP3 standards were prepared at concentrations ranging from 0 to 5,000 pg/mL, whereas the p-tau 217 standards were prepared at concentrations ranging from 0 to 50 pg/mL. The absorbance at 450 nm and 540 nm was measured using the SpectraMax® iD3 multi-mode microplate reader (Molecular Devices, LLC, USA). The concentrations of all markers in each plasma sample were calculated from the corresponding standard curves and expressed as pg/mL. The ELISA kits used in this study included the ELISA MAX™ Deluxe Set Human IL-17A (Cat. No. 433914), Human TNF−α (Cat. No. 430204), Human IFN-γ (Cat. No. 430104), and Human IL-12/IL-23 (p40) (Cat. No. 430704) (BioLegend, USA). ELISA kits for FOXP3 (Forkhead box P3) (Cat. No. orb563391) and p-tau 217 (Cat. No. orb2809907) were obtained from Biorbyt, USA [1].

Measurement of Human Amyloid Beta and Tau Protein Levels

Human Aβ40, Aβ42, total tau, and phosphorylated tau at threonine 181 (p-tau 181) were quantified using the MILLIPLEX Human Amyloid Beta and Tau Magnetic Bead Panel (Merck Millipore), following the manufacturer's instructions. Fluorescence signals were measured with the MAGPIX xMAP Luminex system. The concentrations of each biomarker were calculated from the corresponding standard curves using MILLIPLEX Analyst and Belysa® software [3].

Measurement of Gene Expression

Real-Time PCR (qPCR)

RNA Preparation: Total RNA was extracted from human whole blood using the GenUP™ Blood RNA Kit according to the manufacturer's protocol (Biotechrabbit GmbH, Germany). The RNA concentration and purity were assessed using a NanoDrop spectrophotometer (Thermo Fisher Scientific, USA) [4].

cDNA Synthesis: One microgram of total RNA was converted into cDNA using the iScript™ Reverse Transcription Supermix for RT-qPCR, following the manufacturer's protocol (Bio-Rad). The reaction was performed at 46°C for 20 minutes, followed by enzyme inactivation at 95°C for 1 minute [5-7].

Real-Time Quantitative PCR (RT-qPCR): Real-time quantitative PCR was performed using qPCRBIO SyGreen® Mix Lo-ROX (PCR Biosystems, UK) on an Applied Biosystems™ QuantStudio™ 5 Real-Time PCR System (Thermo Fisher Scientific, USA). The amplification conditions were set according to the manufacturer's instructions. Relative gene expression was calculated using the 2^−ΔΔCt method and normalized to the expression level of GAPDH as the reference gene [5-7]. The primer sequences for autophagy and stem cells are listed in Table 1.

Measurement of Lymphocyte Subpopulations and CD34

Total leukocyte and lymphocyte counts were obtained from complete blood count analysis. The proportion and absolute number of lymphocyte subsets in whole blood were analyzed by flow cytometry using a commercially available kit (BD Multitest™ IMK Kit, BD Biosciences).

Briefly, 100 µL of whole blood was incubated with 10 µL of BD Multitest™ reagent solution in the dark at room temperature for 15 minutes. Erythrocytes were lysed using FACS lysing solution. After 15 minutes of incubation, stained cells were analyzed using a BD FACSCalibur™ (Becton Dickinson, San Jose, CA, USA). The percentages and absolute counts of T cells, CD4+ T cells and CD8+ T cells, were analyzed using FlowJo software (Tree Star, Ashland, OR, USA) [1].

For CD34 enumeration, a BD Trucount™ tube was prepared, and 20 µL of BD Stem Cell Reagent (CD34-FITC/CD45-PE) was added along with 20 µL of 7-AAD viability dye. Using the reverse

Table 1: Primer Sequences.

Gene Name	Forward Primer	Reverse Primer
Autophagy		
LAMP1	CTCTAATGTCTGCAGCTCAAGG	TGTACACAGCGCAGAACAGG
BECN1	GCTCCCGAGGGATGG	AGTAATGGACCTGTGAGTTC
LC3A	CATGAGCGAGTTGGTCAAGAT	TCGTCTTTCTCCTGCTCGTAG
ATG5	TTTGCATCACCTCTGCTTTC	TAGGCCAAAGGTTTCAGCTT
Stem cells		
CD34	AAGCCGAGTAGTGTCTTCCAC	GGGGTAGCAGTACCGTTGTT
CD90	ATGAACCTGGCCATCAGCA	GTGTGCTCAGGCACCCC
CD105	CCACTAGCCAGGTCTCGAAG	GATGCAGGAAGACACTGCTG
NANOG	CTTGGAAGCTGCTGGGGAAGG	ATTACCAACGGTGTCAACCTGC
SOX2	TGGCGAACCATCTCTGTGGTC	ATTACCAACGGTGTCAACCTGC
OCT4 (POU5F1)	GCCACACGTAGGTTCTTGAAT	TGATGTCCTGGGACTGGATTT
GAPDH	TGCACCACCAACTGCTTAGC	GGCATGGACTGTGGTCATGAG

pipetting technique, 100 µL of the blood sample was added to the tube, gently vortexed, and incubated at room temperature in the dark for 20 minutes. Next, red blood cells were lysed by adding 2 mL of Ammonium Chloride Lysing Solution, vortexed again, and incubated in the dark at room temperature for an additional 10 minutes. Finally, the prepared sample was acquired and analyzed using a flow cytometer (BD FACSLyric™).

Measurement of Leukocyte Telomere Length

Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood by density gradient centrifugation. Genomic DNA was extracted from 2–5 million PBMCs using the DNeasy kit (Qiagen), and its purity and quantity were checked via UV spectrophotometry. PBMC telomere length was measured by quantitative PCR (qPCR), comparing the telomere repeat copy number to the single-copy gene 36B4, based on the qPCR method described by O'Callaghan and Fenech [1]. Each 10-µL qPCR reaction included 20 ng of DNA, PowerUp SYBR Green, and telomere primers, with 40 cycles and a dissociation curve for verification. A standard curve ensured reaction linearity ($R^2 > 0.99$) and allowed conversion to absolute telomere length (aTL) in kb per diploid genome. Triplicate runs were used, yielding an interassay variation of 1% [1].

Statistical Analysis

The statistical analyses were performed using GraphPad Prism 6.0, with a significance level of 5% ($p<0.05$) for all analyses.

Results

The initial body composition of the 8 participants is shown in Table 2. The sample group consisted of 8 participants (7 females and 1 male), aged 60-86 years (average age: 70 ± 8 years). Their average body mass index (BMI) was 23.4 ± 2.3 kg/m². All participants were generally healthy, non-drinkers, non-smokers, and had no chronic conditions requiring regular medication. Their daily living activities (diet, exercise, and routine) remained consistent throughout the 8-week data collection period.

During weeks 1-8, 3 capsules of BIM AD® were taken before breakfast and 3 before dinner. All participants experienced no side effects. Food intake and energy expenditure remained consistent throughout the study, as assessed by body composition and blood pressure, which remained stable during the entire period (Table 3).

Table 2: Initial Body Composition of 8 Participants.

No	Sex	Age, yrs	Height, cm	Weight, kgs	BMI,kg/m²
1. J.Sw	F	71	155	62.8	26.1
2. C.As	F	65	157	56.1	22.8
3. N.Sc	F	74	154	58.2	24.5
4. P.Ks	F	69	160	51.0	19.9
5. R.Sk	F	67	157	54.4	22.1
6. S.St	F	60	165	59.2	21.7
7. A.Bj	F	73	152	54.8	23.7
8. S.Rt	M	86	167	74.6	26.7

Table 3: BMI, Body Fat, and Blood Pressure of 8 Participants During the Study.

Parameter	Week	Mean ± SD
BMI, kg/m²	0	23.4 ± 2.3
	4	23.2 ± 2.1
	8	23.2 ± 2.0
Body Fat, % of bw	0	31.9 ± 3.8
	4	30.6 ± 4.0
	8	30.9 ± 4.2
Systolic BP, mmHg	0	128 ± 13
	4	124 ± 18
	8	132 ± 14
Diastolic BP, mmHg	0	75 ± 8
	4	76 ± 8
	8	74 ± 7

Safety of BIM AD®

Effects of BIM AD® on Liver and Renal Function

Kidney function was assessed by measuring BUN and creatinine levels, while liver function was evaluated using SGOT and SGPT enzyme levels. Throughout the study, the levels of serum BUN, creatinine, SGOT, and SGPT, which indicate kidney and liver function, remained within normal ranges (Table 4). Notably, the serum creatinine level at week 8 was significantly lower than that at weeks 0 and 4.

Table 4: Liver and Renal Function Tests of 8 Participants During the Study.

Parameter	Week	Mean ± SD	Normal value
Blood urea nitrogen, mg/dL	0	15.6 ± 5.2	
	4	16.0 ± 3.7	
	8	14.0 ± 3.0	
Creatinine, mg/dL	0	0.95 ± 0.09	Female: 0.65 – 1.08
	4	0.92 ± 0.09	Male: 0.81 – 1.43
	8	0.83 ± 0.09 [a, b]	
SGOT, U/L	0	21 ± 5	Female: 0 – 31
	4	22 ± 4	Male: 0 – 35
	8	20 ± 3	
SGPT, U/L	0	20 ± 10	Female: 0 – 34
	4	19 ± 4	Male: 0 – 45
	8	19 ± 3	

Significant difference from week 0: [a]p<0.0001
Significant difference from week 4 :[b]p< 0.05

Effects of BIM AD® on Stem Cell-Associated Gene Expression

The expression of stem cell-associated genes was evaluated at weeks 4 and 8 and was expressed relative to the week 0 baseline, set at 1.0. Compared with the baseline, treatment with BIM AD® increased the expression of stem cell-associated markers, including CD90, CD105, and CD34, as well as stemness-related genes NANOG, OCT4, and SOX2 (Table 5).

Effects of BIM AD® on CD34 Count

The data demonstrate that the CD34 count progressively and significantly increased from week 0 to weeks 4 and 8 (Table 5).

Table 5: Relative Stem Cell-Associated Gene Expression, % CD34 and CD34 Count of 8 Participants During the Study.

Parameter	Week	Mean ± SD
CD34	0	1.00 ± 0.00
	4	1.43 ± 1.50
	8	4.92 ± 3.59 [a3]
CD90	0	1.00 ± 0.00
	4	1.31 ± 1.33
	8	4.71 ± 3.68 [a3]
CD105	0	1.00 ± 0.00
	4	1.25 ± 1.08
	8	11.27 ± 6.56[a3]
SOX2	0	1.00 ± 0.00
	4	1.79 ± 1.67
	8	6.07 ± 4.81 [a3]
NANOG	0	1.00 ± 0.00
	4	1.64 ± 1.73
	8	5.57 ± 3.93 [a3]
Oct-04	0	1.00 ± 0.00
	4	1.64 ± 1.58
	8	4.82 ± 3.76 [a3]
% CD34	0	0.06 ± 0.05
	4	0.09 ± 0.05[a3]
	8	0.25 ± 0.10[a3, b]
CD34, cells/uL	0	1 ± 1
	4	4 ± 3[a3]
	8	5 ± 3[a1]

Significant difference from week 0: [a1] p < 0.001, [a2] p<0.005, [a3] p<0.05
Significant difference from week 4: [b1]p < 0.05

Effects of BIM AD® on Cytokines

Table 6 summarizes the relative changes in immune parameters (IL-6, IL-10, IL-12/IL-23 (p40), IL-17A, IFN-γ, TNF-α, and FOXP3) among 8 participants across weeks 0, 4, and 8, where all values are normalized to a baseline of 1.00 at week 0. Over the 8-week study period, several parameters demonstrated statistically significant changes compared to baseline and week 4. Specifically, IL-10, IFN-γ, and FOXP3 showed significant increases by week 8, while IL-17A and TNF-α exhibited significant decreases. Meanwhile, IL-6 and IL-12/IL-23 (p40) did not show any statistically significant alterations throughout the monitored intervals.

Table 6: Relative IL-6, IL-10, IL-12/IL-23 (p40), IL-17A, IFN-γ, TNF-α, and FOXP3 of 8 Participants During the Study.

Parameter	Week	Mean ± SD
Interleukin-6	0	1.00 ± 0.00
	4	0.68 ± 0.70
	8	0.80 ± 0.49
Interleukin-10	0	1.00 ± 0.00
	4	0.71 ± 0.33 [a3]
	8	1.55 ± 0.64 [a4, b2]
IL-12/IL-23 (p40)	0	1.00 ± 0.00
	4	0.99 ± 0.12
	8	1.19 ± 0.28
Interleukin 17A	0	1.00 ± 0.00
	4	0.93 ± 0.28
	8	0.67 ± 0.34 [a2, b3]
IFN-γ	0	1.00 ± 0.00
	4	1.25 ± 0.60
	8	2.19 ± 1.40 [a4, b4]
TNF-α	0	1.00 ± 0.00
	4	0.96 ± 0.22
	8	0.67 ± 0.18 [a1, b1]
FOXP3	0	1.00 ± 0.00
	4	1.39 ± 0.61
	8	1.80 ± 0.91 [a4, b3]

Significant difference from week 0: [a1] p<0.002, [a2] p<0.03, [a3] p<0.04, [a4] p<0.05
Significant difference from week 4: [b1] p < 0.02, [b2] p < 0.03, [b3] p < 0.04, [b4] p < 0.05

Effects of BIM AD® on T Cells

Table 7 shows the absolute WBC, lymphocyte, and CD4 and CD8 T-cell counts of 8 participants during the study. There were no changes in these parameters throughout the study.

Effects of BIM AD® on Autophagy Gene Expression

The expression levels of autophagy-related genes were evaluated at weeks 4 and 8 and normalized to the week 0 baseline, which was defined as the reference level (relative expression = 1.0). Compared with baseline, treatment was associated with increased expression of several autophagy-related genes, including ATG5, Beclin-1, LC3, and LAMP. Increased expression was observed in participants with relative expression changes ranging from approximately 1.07-fold to 3.38-fold (Table 8). These findings

suggest that the treatment promotes the activation of autophagy-related processes.

Table 7: Absolute WBC, Lymphocyte, and CD4 and CD8 T-Cell Counts of 8 Participants During the Study.

Parameter	Week	Mean ± SD
White blood cells, cells/uL (4,000 – 10,000 cells/uL)	0	5,610 ± 1,528
	4	5,780 ± 1,040
	8	5,945 ± 1,577
Lymphocyte, cells/uL (1,500 – 4,000 cells/uL)	0	1,836 ± 774
	4	1,772 ± 636
	8	1,775 ± 597
CD4, cells/uL (470 – 1,404 cells/uL)	0	717 ± 366
	4	720 ± 371
	8	717 ± 315
CD8, cells/uL (360 – 1,250 cells/uL)	0	341 ± 112
	4	326 ± 78
	8	323 ± 97

Table 8: Relative Expression Levels of Autophagy-Related Genes of 8 Participants During the Study.

Parameter	Week	Mean ± SD
ATG5	0	1.00 ± 0.00
	4	1.15 ± 0.48
	8	3.38 ± 1.98[a1]
Beclin1	0	1.00 ± 0.00
	4	1.07 ± 0.14
	8	1.87 ± 0.42[a1]
LC3A	0	1.00 ± 0.00
	4	1.72 ± 0.71
	8	2.07 ± 0.59[a1]
LAMP-1	0	1.00 ± 0.00
	4	1.17 ± 0.34
	8	2.16 ± 0.85[a1]

Significant difference from week 0: [a1] $p < 0.05$

Effects of BIM AD® on Leukocyte Telomere Length

An increase in absolute telomere length of 70 base pairs (bp) is equivalent to a one-year reversal in biological age [1]. As shown in Table 9, the mean ± SD of absolute telomere length for all 8 participants was 5,998 ± 1,148 bp at week 0, increasing to 6,022 ± 1,121 bp at week 4 and 6,163 ± 1,117 bp at week 8. The telomere lengths at both week 4 and week 8 increased significantly from week 0. The mean absolute telomere lengths at weeks 4 and 8 increased by 23 and 165 bp from week 0, respectively, equivalent to age reversals of 0.3 and 2.4 years.

Table 9: Leukocyte Telomere Length of 8 Participants During the Study.

Parameter	Week	Mean ± SD
Telomere, base pairs	0	5,998 ± 1,148
	4	6,022 ± 1,121
	8	6,163 ± 1,117 [a2, b1]
Telomere, percentile	0	52 ± 17
	4	54 ± 18
	8	57 ± 18 [a1, b2]

Significant difference from week 0: [a1] $p<0.01$, [a2] $p < 0.02$

Significant difference from week 4: [b1] $p<0.002$, [b2] $p < 0.03$

Effects of BIM AD® on Human Tau Protein and Amyloid Beta Levels

Table 10 displays the relative levels of p-tau 217 from 8 participants measured at weeks 0, 4, and 8, with baseline values normalized to 1.00. Over the course of the study, p-tau 217 levels decreased to 0.93 ± 0.13 at week 4 and further dropped significantly to 0.88 ± 0.12 at week 8.

The relative levels of amyloid-β (Aβ)42/Aβ40 and phosphorylated tau (p-tau 181)/total tau were evaluated in PBMC lysates at baseline (week 0), week 4, and week 8. The relative ratios were normalized to the baseline values at week 0, set to 1.00. The Aβ42/Aβ40 ratio remained comparable to the baseline at week 4 (1.02) but subsequently decreased to 0.85 at week 8. In contrast, the p-tau 181/t tau ratio showed a gradual decrease from 1.00 at baseline to 0.92 at week 4 and further to 0.83 at week 8.

Table 10: Relative P-Tau 217, P-Tau 181/T Tau, and Aβ42/Aβ40 of 8 Participants During the Study.

Parameter	Week	Mean ± SD
P-Tau 217	0	1.00 ± 0.00
	4	0.93 ± 0.13
	8	0.88 ± 0.12 [a2, b1]
P-Tau181/T Tau	0	1.00 ± 0.00
	4	0.92 ± 0.17
	8	0.83 ± 0.11[a1]
Aβ42/Aβ40	0	1.00 ± 0.00
	4	1.02 ± 0.25
	8	0.85 ± 0.23

Significant difference from week 0: [a1] $p < 0.05$, [a2] $p<0.03$

Significant difference from week 4: [b1] $p < 0.04$

Discussion

The expression of stem cell-associated genes was evaluated at weeks 4 and 8 and was expressed relative to the week 0 baseline, set at 1.0. Compared with the baseline, treatment with BIM AD® increased the expression of stem cell-associated markers, including CD90, CD105, and CD34, as well as stemness-related genes NANOG, OCT4, and SOX2. Among these markers, CD90 and CD105 are commonly associated with the mesenchymal stromal cell phenotype [8]. The increased expression of CD90 and CD105 suggests enhanced mesenchymal stem cell-associated characteristics. The upregulation of NANOG, OCT4, and SOX2 indicates increased expression of genes associated with the maintenance of stemness and cellular self-renewal potential [9,10]. Taken together, these findings suggest that BIM AD® supports mesenchymal stem cell-associated cellular maintenance and regenerative capacity.

The hematopoietic stem cell marker (CD34) was also detected and increased with time in the blood samples of all subjects. These stem cells differentiate into macrophages, NK cells, and Th cells. Th cells further change into T regulatory cells in the thymus to

regulate immunity in the body, which is essential in controlling autoimmunity [11-15].

Inflammatory cytokines, IL-17A and TNF-α, showed a significant decrease, which is beneficial for reducing inflammation. The formulation increases FOXP3 (Forkhead box P3), which is a master regulatory protein and transcription factor that is essential for the development, stability, and function of T regulatory cells. It also increases IL-10, which is a key anti-inflammatory protein made by T regulatory cells to modulate the immune system and suppress excessive inflammation.

IFN-γ is primarily secreted by activated Th1 cells, cytotoxic T cells, and natural killer (NK) cells. However, the number of Th1 cells and cytotoxic T cells remains unchanged by this formulation. Thus, the increase in IFN-γ indicates a higher activity or activation of NK cells. In addition, MSCs, together with IFN-γ, shift macrophages from the pro-inflammatory M1 state to the anti-inflammatory, tissue-repairing M2 phenotype [12,13,16-18]. During the study, all participants showed relative expression levels of autophagy-related genes, representing the body's natural cellular recycling and cleaning system that breaks down and reuses damaged cell parts.

Telomeres of all participants were lengthened mainly by the increase in new stem cells stimulated by the formulation.

Most importantly, while amyloid-β showed little difference, p-tau 217 and the p-tau 181/t tau ratio were significantly reduced, indicating a definite reduction in AD-related conditions.

This evidence strongly indicates that this formulation, BIM AD®, is beneficial for remedying inflammation and degeneration in all systems of the body, particularly for AD.

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