

THE IMPORTANCE OF SLEEP QUALITY IN A NIGHT-TIME SKIN CARE REGIME

What is Mighty Night™ and How Does it Work?

Mighty Night™ dietary supplement has been formulated to support both night-time skin cell recovery and promote good sleep. Designed to be taken before bedtime, Mighty Night™ helps to support skin cell turnover during sleep, scavenge free radicals, boost sleep quality and improve skin tone.

The primary function of skin is to create a barrier between internal organs and the outside environment, and to retain water. Skin naturally undergoes chronological aging due to environmental factors, especially in areas, such as the face, that are exposed daily to stresses such as UV radiation and pollution. Chronological aging is also associated with decreased epidermal lipids, loss of which causes dry skin and, eventually, fine wrinkles, lines, and cracks. These lipids -- including phospholipids, ceramides, cholesterol, cholesterol esters, cholesterol sulfate, triglycerides, and fatty acids -- have major roles in cell structure, control of growth, and skin permeability.¹

Circadian rhythms control many cellular functions and other biological processes. Physiological changes during sleep allow stem cells to proliferate, controlled by circadian clock genes or indirectly by hormones and growth factors. Hormones such as melatonin and cortisol regulate many biological functions during sleep.² When quality of sleep is diminished, hormone levels can be altered, causing additional stress on the body. Sleep helps to regulate normal human hormone levels and metabolism, and studies have shown that sleep plays a role in restoring immune system function and that changes in the immune response may affect collagen production. Poor quality sleep can also contribute to signs of aging such as wrinkles and other alterations in pigmentation. Studies which identify poor sleep quality as a factor in compromised skin health suggest it is important to consider improvements in sleep quality as part of maintaining a healthy skin.³ Chronic poor sleep quality is associated with increased signs of intrinsic ageing, diminished skin barrier function and lower satisfaction with appearance.⁴

To support overnight skin cell recovery, Mighty Night™ contains wheat-derived ceramides, similar to the lipid molecules which form key components of human skin dermis and epidermis layers. Ceramides taken orally can affect skin appearance by providing both cell protection and increased hydration.

Mighty Night™ is also formulated with ferulic acid, which possesses antioxidant properties, and ubiquinol, the most absorbable form of CoQ10, a fat-soluble antioxidant which helps to protect cells from the damage caused by free radicals. Ubiquinol scavenges free radicals generated within liposomal membranes and can prevent oxidative damage to epidermal lipids.

¹ Semin Dermatol. 1992 Jun;11(2):106-13. Epidermal lipids. Wertz PW.

² Tissue regeneration: Impact of sleep on stem cell regenerative capacity. Hoda Elkhenany, Abdelrahman AIOkda,Ahmed El-Badawy, Nagwa El-Badri. Life Sciences: Elsevier Published 1 December 2018

³ Guan L., Mehra R., Baron E. (2017) Sleep and Aging Skin. In: Farage M., Miller K., Maibach H. (eds) Textbook of Aging Skin. Springer, Berlin, Heidelberg

⁴ Medical Hypotheses, Volume 75, Issue 6, 2010, Pages 535-537. Can poor sleep affect skin integrity? V. Kahan, M.L. Andersen, J. Tomimori, S. Tufik.

Support for improved sleep quality is provided in Mighty Night™ by a blend of botanical extracts, including passionflower, valerian, and hops, which have been used as traditional herbal sleep aids for many centuries.

INGREDIENTS OF MIGHTY NIGHT™

Ingredients for Repairing Damaged Skin

Wheat Ceramides™

Mighty Night™ contains 70 mg per serving of a patented, gluten-free, lipid extract of wheat seed (*Triticum vulgare* L.) which contains both wheat ceramides and wheat digalactosyldiglycerides, which have the effect of boosting the activity of the ceramides.

The lipid matrix in the outermost layer of the skin, the stratum corneum, is crucial for skin barrier functions such as preventing excessive water loss through the epidermis and protecting against compounds from the environment permeating into the epidermal and dermal layers. The composition of the stratum corneum lipid matrix is dominated by three lipid classes: cholesterol, free fatty acids and ceramides.⁵

Ceramides are known to play a key role in the skin's barrier function. An age-dependent decrease in ceramides content correlates with cutaneous signs of dryness, loss of elasticity, and increased roughness. Cosmetic research has traditionally focused on the topical application of ceramides and/or sphingolipids to the skin. More recently, scientists have investigated the beneficial effects of oral supplementation with ceramides to improve dry skin and skin appearance. A double-blind, placebo-controlled, randomized study⁶ on sixty healthy Caucasian female subjects with dry skin, skin aging related to photoaging, or mild-to moderate chrono-aging showed that daily oral supplementation of purified wheat glucosylceramides and digalactosyldiglycerides induced a strong and highly significant improvement in skin hydration markers compared to placebo, after only 15 days and beyond.

Ceramides represent 35-40% of the intercellular cement binding cells together and contributing to skin hydration. A wheat extract oil (WEO) rich in ceramides and digalactosyldiglycerides was used in a double-blind, randomized, placebo-controlled study⁷ on 51 women aged 20-63 years with dry to very dry skin who received either 350 mg of WEO or placebo for 3 months. Perceived efficacy was noted by

⁵ Stratum Corneum Lipids: Their Role for the Skin Barrier Function in Healthy Subjects and Atopic Dermatitis Patients. Agner T (ed): Skin Barrier Function. Curr Probl Dermatol. Basel, Karger, 2016, vol 49, pp 8-26.

⁶ Bizot, V.; Cestone, E.; Michelotti, A.; Nobile, V. Improving Skin Hydration and Age-related Symptoms by Oral Administration of Wheat Glucosylceramides and Digalactosyl Diglycerides: A Human Clinical Study. *Cosmetics* **2017**, *4*, 37.

⁷ Guillou, S. , Ghabri, S. , Jannot, C. , Gaillard, E. , Lamour, I. and Boisnic, S. (2011), The moisturizing effect of a wheat extract food supplement on women's skin: a randomized, double-blind placebo-controlled trial. *International Journal of Cosmetic Science*, 33: 138-143.

participants throughout the study; skin hydration was significantly increased on the arms ($P < 0.001$) and legs ($P = 0.012$) in the WEO group compared with placebo.

Antioxidants and Free Radical Scavengers

Ubiquinol

Ubiquinol, a fat-soluble antioxidant, protects cells from the damage caused by free radicals. This damage can contribute to various diseases and premature aging. The conventional, ubiquinone form of CoQ10 is less bioavailable⁸ than ubiquinol. Mighty Night contains 25 mg of absorbable ubiquinol (KANEKA QH) per serving.

Ubiquinone in its reduced form -- ubiquinol – acts as an antioxidant⁹. Its high degree of hydrophobicity and widespread occurrence in biological membranes suggest ubiquinol plays an important role in cellular defenses against oxidative damage. Aging skin, among other symptoms, may be a consequence of a decreased capacity to maintain adequate ubiquinol levels.

Trans-Ferulic Acid

Mighty Night™ contains 100 mg of trans-ferulic acid per serving. Trans-ferulic acid is a phenolic phytochemical which is abundantly present in plant cell walls. In a study¹⁰, the antioxidant activity of 24 ferulic acid-related compounds was evaluated, as well as their role in radical scavenging activity, using several different physical systems. Ferulic acid was most effective among the tested phenolic acids; results indicated that not only the radical scavenging ability of antioxidants, but also their affinity with lipid substrates, might be important factors in their activity.

Ingredients for Improved Sleep Quality

Research¹¹ has indicated that circadian rhythms affect cell function in human epidermal stem cells and that disturbance of these rhythms can therefore contribute to aging. Established, regular sleep patterns are essential to promote general good health and skin repair. To support and improve sleep quality and allow skin to regenerate, Mighty Night™ contains valerian root, passionflower, and hop flower extracts.

⁸ Clin Pharmacol Drug Dev. 2014 Jan;3(1):13-7. Comparison study of plasma coenzyme Q10 levels in healthy subjects supplemented with ubiquinol versus ubiquinone. Langsjoen PH, Langsjoen AM.

⁹ Ubiquinol: an endogenous antioxidant in aerobic organisms. Ernster, L. & Forsmark-Andrée, P. Clin Investig (1993) 71(Suppl 8): S60.

¹⁰ Antioxidant Properties of Ferulic Acid and Its Related Compounds. Hiroe Kikuzaki,* ,†, Masashi Hisamoto,†, Kanae Hirose,†, Kayo Akiyama,† and, and Hisaji Taniguchi‡ Journal of Agricultural and Food Chemistry 2002 50 (7), 2161-2168

¹¹ Human Epidermal Stem Cell Function Is Regulated by Circadian Oscillations. Peggy Janich et al. Cell Stem Cell 13, 745–753, December 5, 2013

A double-blind, randomized, controlled trial¹² assessed the efficacy and safety of a polyherbal formulation containing standardized extracts of valerian (*Valeriana officinalis*), passionflower (*Passiflora incarnata*) and hops (*Humulus lupulus*) in comparison with zolpidem (Ambien™). A total of 91 subjects were recruited, of which 39 in each group completed the study. There was significant improvement in total sleep time, sleep latency, number of nightly awakenings and insomnia severity index scores in both groups.

Valerian Root Extract

Mighty Night contains 150mg of valerian root extract per serving. Valerian is a flowering plant which has been used as a traditional herbal sleep aid for over 2000 years¹³, and extracts of valerian root have been widely used in Europe to treat sleeping disorders for decades. The German E Commission monograph¹⁴ describes valerian root as consisting of fresh underground plant parts of the species *Valeriana officinalis* and its preparations. The roots contain essential oils with monoterpenes and sesquiterpenes (valerenic acids). The EU Committee on Herbal Medicinal Products (HMPC) also concluded that, based on its long-standing use, valerian root preparations can be used for relief of mild symptoms of mental stress and to aid sleep.

Sleep disturbances can significantly reduce quality of life and the body's ability to repair tissues and organs. A study¹⁵ to investigate whether poor sleep quality affects skin ageing indicated that chronic poor sleep quality is associated with increased signs of intrinsic ageing, diminished skin barrier function and lower satisfaction with appearance. Another study¹⁶ indicated that valerian improves the quality of sleep in women with menopause who are experiencing poor sleep patterns.

In a study¹⁷, 128 volunteers were given 400 mg of an aqueous extract of valerian, a commercial preparation containing 60 mg valerian and 30 mg hops, and a placebo. Participants took each one of the three preparations three times in random order on nine nonconsecutive nights and filled out a questionnaire the morning after each treatment. Compared with the placebo, the valerian extract resulted in a statistically significant subjective improvement in time required to fall asleep (more or less difficult than usual), sleep quality (better or worse than usual), and number of nighttime awakenings

¹² Maroo N, Hazra A, Das T. Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: A randomized controlled trial. *Indian J Pharmacol* 2013;45:34-9

¹³ American Herbal Pharmacopoeia, Valerian Root *Valeriana officinalis* Analytical, Quality Control, and Therapeutic Monograph, April 1999, Ed. Roy Upton.

¹⁴ Blumenthal, M., & Busse, W. R. (1998). The complete German Commission E monographs. Austin, Texas: American Botanical Council.

¹⁵ Oyetakin-White, P., Suggs, A., Koo, B., Matsui, M. S., Yarosh, D., Cooper, K. D. and Baron, E. D. (2015), Does poor sleep quality affect skin ageing?. *Clin Exp Dermatol*, 40: 17-22.

¹⁶ Effect of valerian on sleep quality in postmenopausal women: a randomized placebo-controlled clinical trial: Simin Taavoni et al. *Menopause: The Journal of The North American Menopause Society* Vol. 18, No. 9, pp. 951/955

¹⁷ Leathwood PD, Chauffard F, Heck E, Munoz-Box R: Aqueous extract of valerian root (*Valeriana officinalis* L.) improves sleep quality in man. *Pharmacology, Biochemistry and Behavior* 17: 65-71, 1982.

(more or less than usual). This result was more pronounced in a subgroup of 61 participants who identified themselves as poor sleepers on a questionnaire administered at the beginning of the study.¹⁸

Passionflower Extract

Mighty Night™ contains 80 mg passionflower (aerial parts) standardized to 3.5% vitexin, per serving. Passionflower is a perennial creeping vine, native to the tropical and semi-tropical southern United States, Mexico, and Central and South America. Passionflower was first cultivated by native Americans for its edible fruit. Spanish conquerors first learned of passionflower from the Aztecs of Mexico who used it to treat insomnia and nervousness; the plant was taken back to Europe where it became widely cultivated and introduced into European herbal practice. It is a component of a standard German Commission E¹¹ fixed formula 'Sedative Tea,' which contains 40% valerian root, 30% passionflower herb, and 30% lemon balm leaf. In the United States, passionflower is used as a sedative component of dietary supplement sleep aid formulations. Passionflower is frequently used in combination with valerian and other sedative plants¹⁹. ESCOP²⁰ indicates its use for tenseness, restlessness, and irritability with difficulty in falling asleep.

Hop Flower Extract

Mighty Night™ contains 30 mg of hop flower extract (*Humulus lupulus* L.) A climbing perennial herb with male and female flowers on separate plants, hops are native to Europe, Asia, and North America. The therapeutic use of hops in Europe dates to at least the ninth century. In North America, the Cherokee traditionally used hops as a sleep aid; in India, the Ayurvedic Pharmacopoeia recommends hops for restlessness associated with nervous tension, headaches, and indigestion.

Human studies have researched the use of hops in combination with other herbs (e.g., valerian root). One study examined the effects of dry extracts of hop strobile and valerian root on subjects with sleep disturbances. The study reported that hops lessened sleep disturbances when given in combination with valerian. However, it was not possible to determine if the action was caused by the hops, the valerian, or a possible synergy between the two. Though the sleep-inducing effect of hops is indisputable, its mechanism of action is not yet fully understood.¹¹

MIGHTY NIGHT EVALUATION STUDY

Methodology

Twenty-seven participants were recruited based on skin care and sleep concerns. Many participants reported having trouble sleeping and wanted to see an improvement in fine lines, wrinkles, and skin

¹⁸ Valerian: Fact Sheet for Health Professionals. NIH/ODS. Accessed 10/4/19
<https://ods.od.nih.gov/factsheets/Valerian-HealthProfessional/#en13>

¹⁹ Bradley, P.R. (ed.). 1992. British Herbal Compendium, Vol. 1. Bournemouth: British Herbal Medicine Association.

²⁰ European Scientific Cooperative on Phytotherapy (ESCO)

hydration. The participants ranged from 26-55 in age, were given nutrition and lifestyle guidance, and instructions on how to take the Mighty Night product. Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI)²¹ at baseline, 30 and 60 days. Skin was assessed using the VISIA system²² which provides analysis of eight different skin conditions using multi-spectral lighting and a comparison algorithm. The study also used self-reported data and the Moritex Moist Sense²³ meter at baseline and 60 days.

RESULTS

Skin Appearance

Over 80% of the participants who evaluated MIGHTY NIGHT for 60 days agreed that their skin’s overall appearance had improved during that time. Participants indicated that their skin looked brighter and smoother with a natural glow and agreed with the statement that MIGHTY NIGHT helped their skin to look its best from the inside out.

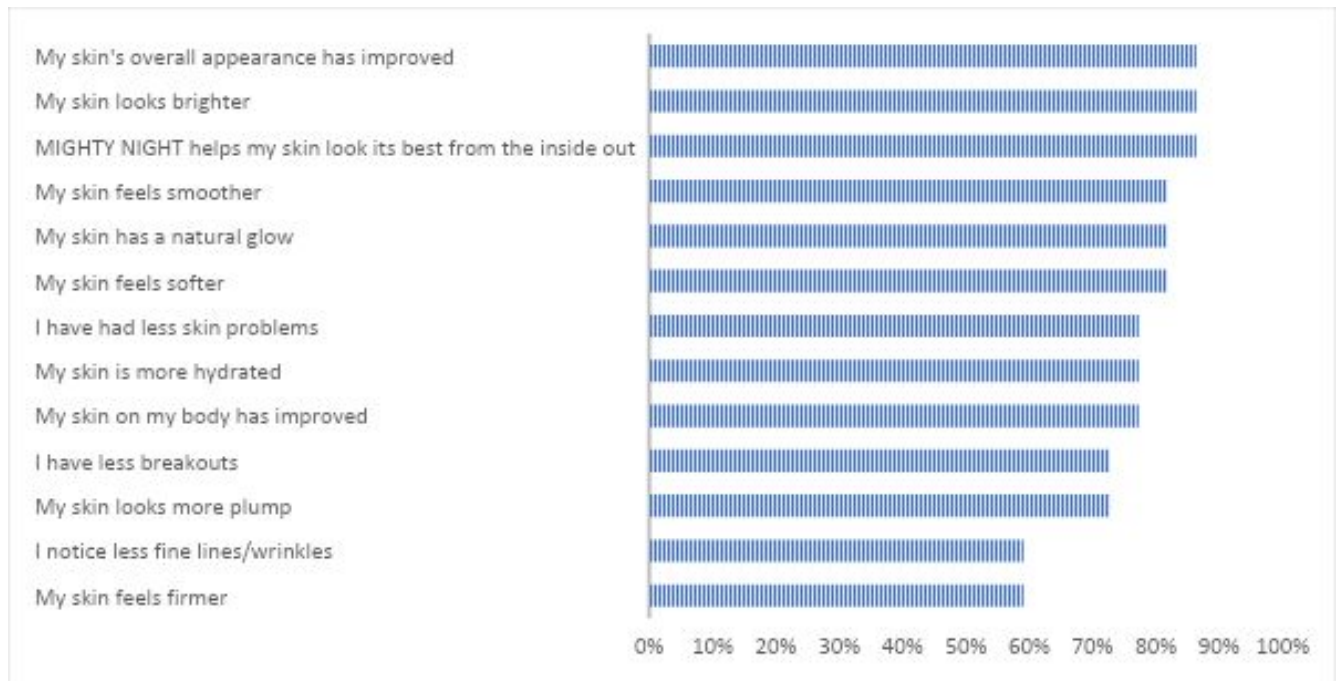


Figure 1: Percentage of participants who agree or strongly agree with the survey statement after 60-day treatment. Source: HUM Nutrition Inc.

²¹ Buysse, D.J., Reynolds, C.F., Monk, T.H., Berman, S.R., & Kupfer, D.J. (1989). The Pittsburgh Sleep Quality Index (PSQI): A new instrument for psychiatric research and practice. *Psychiatry Research*, 28(2), 193-213

²² Canfield VISIA® Skin Analysis System <https://www.canfieldsci.com/imaging-systems/visia-complexion-analysis/> Accessed 11/11/2019

²³ Moritex Moist Sense http://moritex.com/products/counseling_system/skin_sensor/index.html Accessed 11/11/2019

Figure 1 shows the percentage of participants who agreed or strongly agreed with questionnaire statements in a 60-day trial of Mighty Night™ dietary supplement, taken orally for 60 days. Total participants: 27.

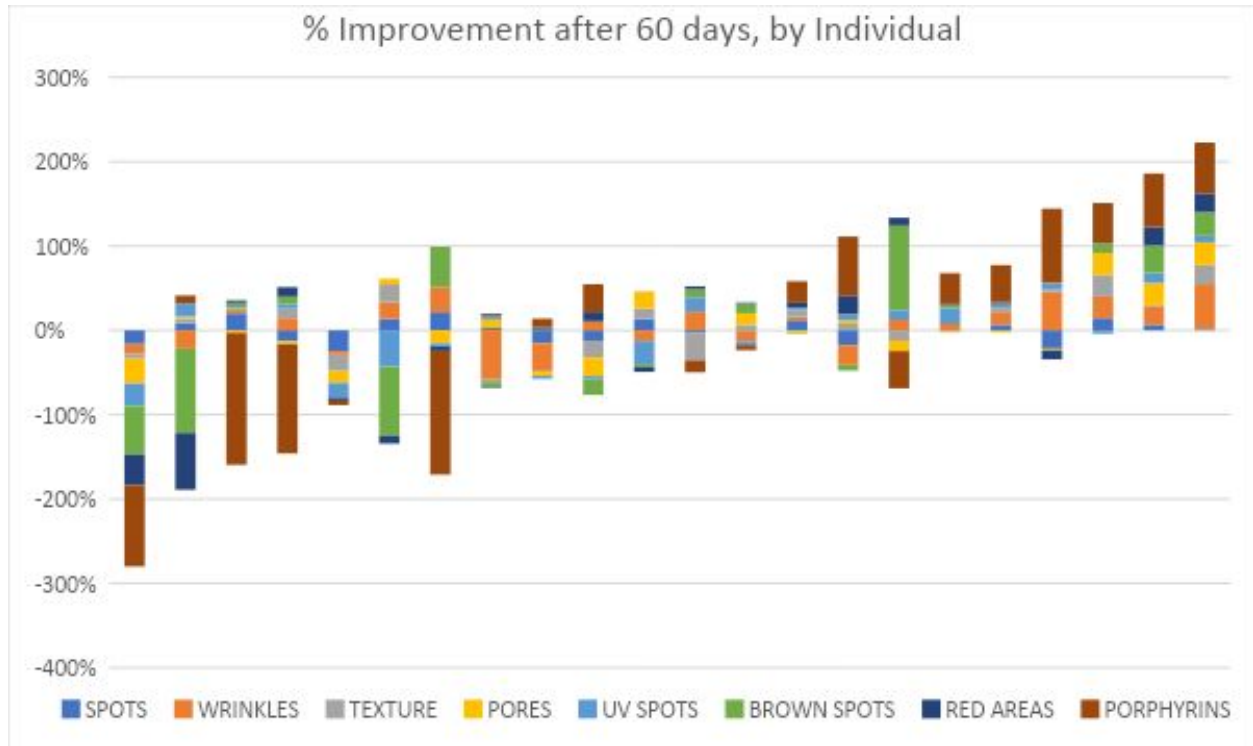


Figure 2: Results of Visia system™ analysis after 60 days. Source: HUM Nutrition Inc.

Figure 2 shows that skin results as measured by the Visia system were inconclusive. Most participants who completed this part of the study showed improvement in one or more measures. Fifty percent of participants experienced overall improvement, while others experienced no improvement, or deterioration, in some or all measures of skin appearance after 60 days.

Sleep Quality

Study participants experienced MIGHTY NIGHT™'s sleep benefits; they were evaluated using the PSQI which is used to measure quality and patterns of sleep. The PSQI differentiates sleep quality by measuring seven subjective sleep quality indexes, including sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. A higher score indicates poorer sleep quality. Average PSQI scores dropped at 30 days and again at 60 days.

	DAY 0 (baseline)	DAY 30	DAY 60	% Chang e day 0 to 30	% Chang e day 0 to 60

AVERAGE TIME TO GET TO SLEEP MINUTES	39	26	18	-34%	-54%
AVERAGE TIME SPENT SLEEPING HOURS	5.94	6.67	7.09	12%	19%
AVERAGE PQSI SCORE	11	6	3	-45%	-71%

Table 1: Sleep data at baseline, 30 days and 60 days. Source: HUM Nutrition Inc.

Table 1 show that participants experienced, on average, 34% shorter times to get to sleep, 12% more time spent sleeping, and much lower average PQSI scores after 30 days. Further improvements of 54% less time to sleep, and 19% more time spent sleeping were experienced after 60 days of taking Mighty Night™.

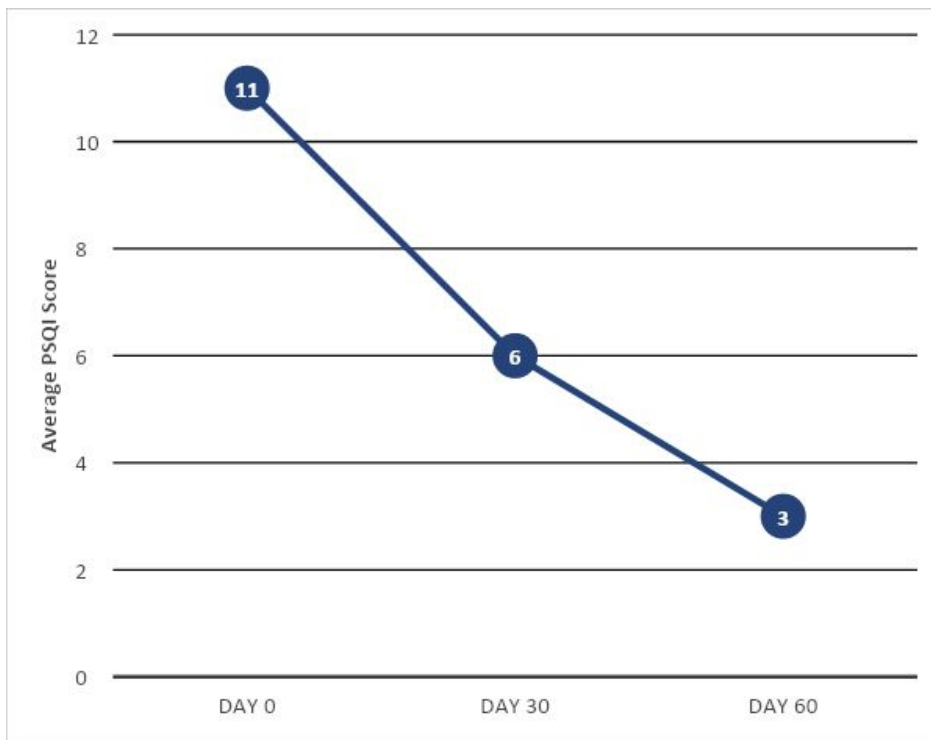


Figure 3: Average participant PSQI sleep quality scores at baseline, 30 days and 60 days. Source: HUM Nutrition Inc.

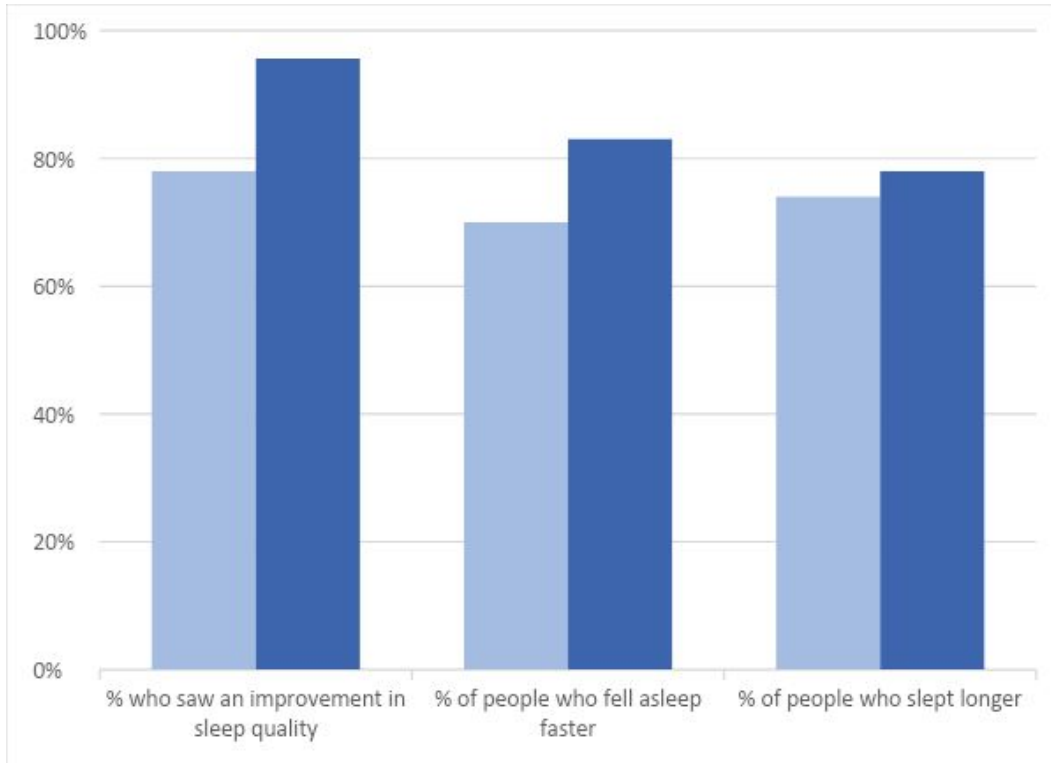


Figure 4: Percentage of participants who saw improvements in sleep quality in a 60-day trial of Mighty Night™ dietary supplement, taken orally for 60 days. Source: HUM Nutrition Inc.

Figure 4 illustrates that 96% of study participants saw an improvement in their sleep quality index score after 60 days; over 80% fell asleep faster, and nearly 80% slept longer while taking MIGHTY NIGHT™.

CONCLUSIONS

Mighty Night™ achieves its benefits in two ways: promotion of overnight skin renewal and improved sleep quality. These two effects work in tandem to help improve skin appearance over time. The supplement is formulated with ingredients that help support skin composition, improve structure, and can help to repair damage caused by normal aging, exposure to UV, and other environmental factors. A survey involving a group of volunteers showed that both skin and sleep benefits could be perceived by the participants after 60 days of oral supplementation with Mighty Night™.