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Development and Verification of a 480 nm Blue Light Enhanced/Reduced Human-Centric LED for Light-Induced Melatonin Concentration Control

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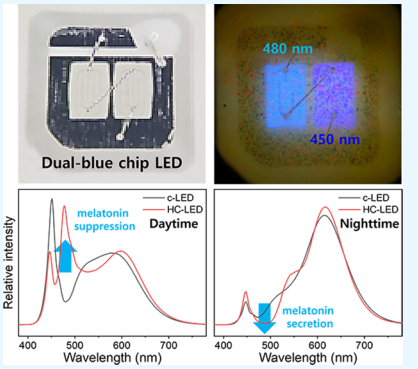
ABSTRACT: With the inherent sleep and wake cycle regulated by natural sunlight, the human body has evolved over millennia to be active during the day and to rest at night. However, maintaining an optimal 24 h cycle has become increasingly problematic in modern society as more people spend the majority of the day indoors. Many research groups have reported that inadequate artificial lighting interferes with melatonin production and disrupts the circadian rhythm. This study considered biological functions for light-emitting diodes (LEDs) of next-generation illumination, and LED packages and spectra suitable for both daytime and nighttime applications were designed. The prepared daytime human-centric (HC)-LEDs had a melanopic/photopic (M/P) ratio that was up to 26% higher than that of conventional (c)-LEDs, whereas the nighttime HC-LEDs exhibited up to a 26% lower M/P ratio compared to the c-LEDs. Nevertheless, because the HC-LED is designed to have almost the same color coordinates as the c-LED having the same correlated-color temperature (CCT), there is no change in the perceived color. To substantiate the biological effect, melatonin level data were obtained from 22 voluntary participants in c- and HC-LED lighting environments. In the HC-LED lighting environment, melatonin was suppressed by 21.9% after waking, and nocturnal melatonin secretion was increased by up to 12.2%. As human-centric lighting, our HC-LEDs are expected to become an essential element for modern life, where people spend most of their time indoors.



1. INTRODUCTION

Light can visually and nonvisually affect humans through the eyes' retinal cells. The secretion of hormones such as melatonin and the resulting circadian rhythm can be physiologically altered by the nonvisual effects of light.[1−3] Until the discovery of retinal melanopsin in intrinsically photosensitive retinal ganglion cells (ipRGCs) of mammals[4,5] and humans,[6,7] only the effect of light on the cones and rods of the retina cell photoreceptors on providing as visual information was known. As photoreceptors, ipRGCs are particularly sensitive to the absorption of blue light with a wavelength of 480 nm. There is evidence that radiation within the 460 to 500 nm wavelength can regulate the circadian rhythm for a natural day to night cycle.[8] In this context, bright light with a wavelength of 460 to 500 nm during the evening and night in terms of its effects on melatonin levels is considered unsuitable for proper relaxation and sleep. Disruption of a traditional nighttime circadian rhythm can be explained by exposure to the wrong kind of light at an inappropriate time.[9,10] Because the human biological clock is promptly synchronized with the natural light−dark cycle, it is critical for people in today's modern world to use or be exposed to light properly. The biological clock is influenced by exposure to light and affects hormones, (core) body temperature, and sleep.[11−15]

Over the last two decades, solid-state lighting (SSL)-based phosphor-converted lighting-emitting diodes (pc-LEDs) have evolved extensively because of their potential and/or practical applications in backlight units for liquid crystal displays (LCDs), traffic lights, and general illumination, including indoor and outdoor lamps. LEDs have been adopted on the basis of satisfactory performance such as low power consumption, high brightness, small size, fast response time, and long lifetime.[16,17] To date, most LED lighting development has been focused on energy performance and color qualities of white LEDs such as high luminous efficacy (LE), high color rendering index (CRI), and low power consumption.[18,19] However, these optical and energy-saving properties fail to represent the full performance potential of

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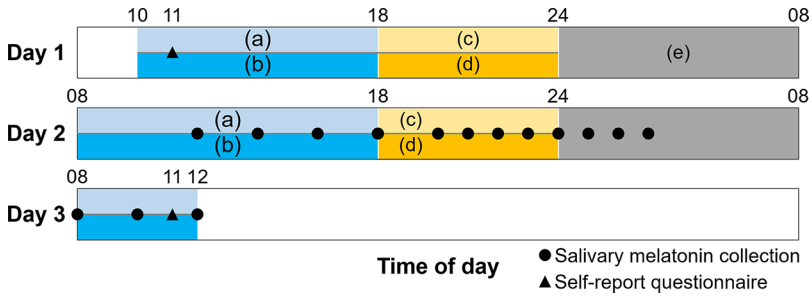

Figure 1. Fifty hour experimental schedules. Participants were admitted to the clinical laboratory at 10:00 on the first day and left at 12:00 on the third day. The lighting conditions were divided into conventional lighting and human-centric lighting (HCL). (a) Daytime conventional lighting and (b) daytime HCL with correlated-color temperature (CCT) of 5000 K. (c) Nighttime conventional lighting and (d) nighttime HCL with CCT of 2200 K. (e) Light off and sleep. All participants took part in the experiment with an interval of 1 week for both types of lighting. The black solid circles and triangles represent salivary sampling time and the questionnaire responses for assessing subjective drowsiness.

LED lighting. In particular, a significant number of people spend up to 90% of their time under indoor electrical lighting.[20] This means that, during the day, we can be exposed to bright artificial lighting with radiation energy of approximately 480 nm wavelength, which is equivalent to a sufficient dose of actual daylight. This specific light, which is associated with melatonin suppression and secretion, can be applied to functional artificial lighting to regulate alertness, sleep, and the circadian rhythm.[21−23]

The attention of many researchers is shifting from the performance of lighting in terms of energy to lighting quality that can affect human productivity, comfort, mood, safety, and health.[24] As such, many researchers and experts have thought about lighting as "circadian lighting", "biological lighting", and "human-centric lighting (HCL)". Some studies have offered evidence and support of a high CRI, the convenience of smart lighting, low glaring lighting, and melatonin related lighting for HCL.[25] Furthermore, to produce a lighting effect on the human body, there are various ways to adjust the correlated-color temperature (CCT) using warm-white (WW), cool-white (CW), and near-ultraviolet (n-UV) LEDs, similar to the sunlight spectrum.[26] In this study, we developed LED packages focused on blue light with a wavelength of 480 nm, which is directly related to melatonin secretion and suppression, as HCL. Because the melatonin concentration should be maintained differently during the daytime and nighttime, our human-centric (HC)-LEDs were developed separately for daytime and nighttime. White HC-LED packages containing two blue chips emitting light with a wavelength of 450 and 480 nm were implemented to have a total 12 types of CCT depending on the application. In addition, HC-LED packages have almost the same color coordinates as conventional LED (c-LED) packages having the same CCT, and hence, there is no change in perceived color. Ultimately, to verify the nonvisual effects of the developed LED package, melatonin level data from 22 voluntary participants were collected under c- and HC-LED lighting environments with the same illuminance and CCT. The melatonin concentration analysis results indicate that the light-induced melatonin control was more effective in the HC-LED lighting environment with a regulated wavelength of 480 nm considering the circadian rhythm than in the c-LED lighting environment. Therefore, the daytime and nighttime HC-LEDs can be sufficiently used for indoor lighting from a human point of view rather than from an energy point of view, and HC-LEDs can help to enhance the circadian rhythm of people today who spend most of their time indoors.

2. EXPERIMENTAL SECTION

2.1. LED Package and Spectral Design. The LED package design consists of two chips: (1) a chip emitting light with a wavelength of 470 to 480 nm for melatonin suppression and secretion control and (2) another chip emitting light with a wavelength of 445 to 455 nm to secure the original optical properties of a blue light emitter. The spectral designs varied from WW with a CCT of 1800 K to CW with a CCT of 6500 K. The designed LED package was divided into two types of LEDs according to the usage time period: (1) daytime LEDs with a CCT of 3000 to 6500 K were designed to rapidly suppress melatonin immediately after waking up and improve subjective drowsiness, and (2) nighttime LEDs with a CCT of 1800 to 4000 K were designed to activate melatonin secretion at night. For all types of LEDs, a CRI of >80 was achieved. The characteristics of the prepared dual-blue-chip LEDs were evaluated using an integrating sphere with a diameter of 300 mm by applying a current of 150 mA. The melanopic/photopic (M/P) ratio, which is considered the ratio of magnitude of nonvisual effects of the developed LED, was compared with that of a c-LED series (LM302Z+, Samsung Electronics, Co., Ltd., Korea) with the same package structure, power consumption, and CCT (see Table S1). The M/P ratio is expressed by the following equation:[27]

$$\mathrm{M/P ratio} = \frac{72983.25 \int E_{e,\lambda}(\lambda) N_z(\lambda) d\lambda}{K_m \int E_{e,\lambda}(\lambda) V(\lambda) d\lambda} \quad (1)$$

where $E_{e,\lambda}(\lambda)$ is the spectral irradiance, $N_z(\lambda)$ is the melanopic sensitivity curve, $V(\lambda)$ is the photopic spectral luminous efficiency function, and K_m is the maximum spectral luminous efficacy of 683.002 lm/W.

2.2. Participants. To confirm the effect on circadian rhythm, this study was conducted with 22 Korean health male volunteers, and there were no female participants. The average age of the participants was 27.4 ± 4.36 years (mean ± SD). The self-reported questionnaires, in this case, the Korean version of the Pittsburgh Sleep Quality Index (PSQI-K)[28] and Epworth Sleepiness Scale (ESS),[29] were administered to participants 1 week prior to admission; PSQI-K was 6.4 ± 1.2 in the range of 4 to 8, and ESS was 5.7 ± 2.7 in the range of 1 to 10. In PSQI-K, the cutoff score between good and poor sleepers was modified from 5 to 8.5 in the process of adapting the conventional PSQI into Korean.[28] Therefore, all participants were considered to have a normal circadian rhythm. In addition, according to the responses to the self-

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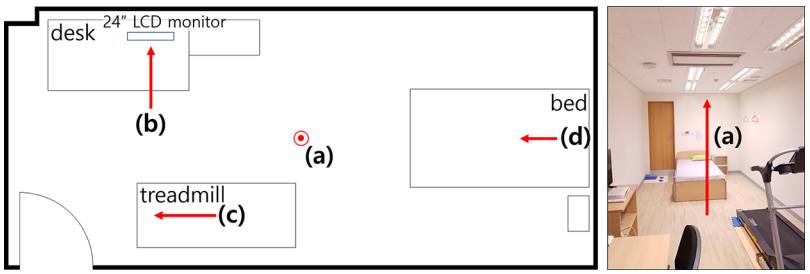

Figure 2. Schematic of a room where the 50 h protocol was performed and locations of the illuminance measurement. (a) Measured toward the lighting at 85 cm from the floor in the center of the room. (b) Measured toward the center of the monitor at 120 cm from the floor and 70 cm from the monitor. (c) Measured toward a facade wall at 170 cm from the floor. (d) Measured toward a regular book positioned 40 cm below 45° at 120 cm from the floor. The dimension of the room was L 6640 mm × W 2880 mm × H 2480 mm.

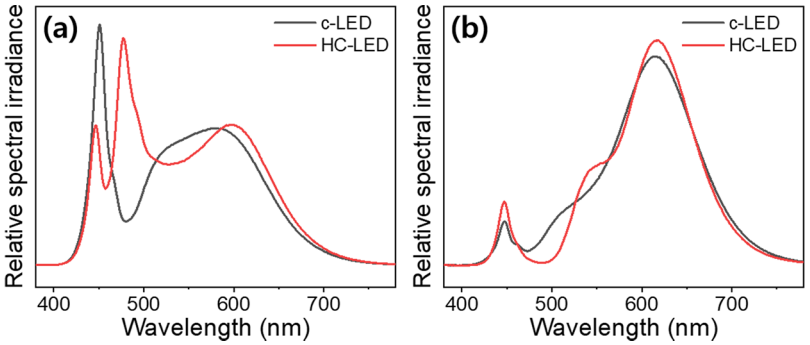

Figure 3. Comparison of relative spectral irradiance of c- and HC-LEDs at (a) daytime with a CCT of 5000 K and (b) nighttime with a CCT of 2200 K. c-LED, conventional LED; HC-LED, human-centric LED.

reported questionnaire, the 22 participants went to bed at 00:51 ± 00:23 and woke at 08:30 ± 00:13. The participants had confirmed the research information in advance, provided written consent to participate in the study, and received a participation fee upon completing all procedures as requested. To accurately assess the effects of light on the circadian rhythm, individuals who fell into specific categories were excluded from the study. These included anyone ingesting medication related to chronic or neurological disease, those who had traveled internationally within 4 weeks prior to the study, and those who had an irregular bedtime within 3 months before the study due to night shift work.

2.3. Experimental Protocol. The experiment was conducted at the Hybrid Device-Based Circadian ICT Research Center (C-ICT), Kookmin University, from January 2019 to December 2019. One week prior to the start of the study, the participants were instructed to maintain their habitual sleep−wake pattern. This study was conducted with one participant at a time in two 50 h sets (conventional lighting and HCL) in a temperature and relative humidity controlled clinical laboratory, as shown in Figure 1. In particular, in this study, the constant routine (CR) protocol, which includes the time-consuming dim light condition, was intentionally excluded to make light-induced melatonin control more accessible to those interested. All participants were exposed to both types of lighting with an interval of 1 week, and the first type of lighting was randomly assigned to each participant (half of all participants started with conventional lighting). The participants arrived at the experimental chamber before 10:00 on the first day and were exposed to both daytime and nighttime lighting conditions. Both daytime and nighttime lighting conditions were controlled, as the timelines required different roles for melatonin. After 8 h of sleep in darkness, participants woke up at 08:00 and followed a full day's schedule and left at 12:00 on the third day after being exposed to the daytime light condition from 08:00 to 12:00. Because the participants were exposed to different light in their own space prior to admission, they spent time adapting to the designed lighting on the first day to minimize the effects of this light. There were no restrictions on their behavior when staying inside the laboratory. Electronic video devices such as a computer or smartphone could be used with application of a blue light filter, but the device use was restricted from 18:00 until bedtime. All meals were served at the same times (08:00, 13:00, and 18:00) and were the same food type. During the application of each experimental condition, saliva samples were collected 15 times to measure melatonin levels depending on lighting. Melatonin samples were collected every 2 h from 12:00 to 20:00, every hour from 20:00 to 03:00 on the second day, and every 2 h from 08:00 to 12:00 on the third day. The Stanford Sleepiness Scale (SSS) was administered at 11:00 on the first day and third day to assess the subjective sleepiness of the participants.[30] The study was conducted according to the guidelines of the Declaration of Helsinki, and the study protocols were approved by the Kookmin University Institutional Review Board (KMU-201904-HR-203).

2.4. Lighting Conditions. The lighting was installed in the ceiling of the clinical laboratory, where natural light was completely blocked, and the light was emitted directly into the room, as shown in Figure 2. Because the developed human-centric LED (HC-LED) packages were categorized into daytime and nighttime use according to the M/P ratio, a total of four lighting conditions, including the conventional LEDs (c-LEDs) with the same CCT, were constituted together in one luminaire and controlled through a smart lighting platform kit. During the daytime from 08:00 to 18:00 and

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nighttime from 18:00 to 00:00, the CCT was fixed at 5000 and 2200 K, respectively. The M/P ratio of the HC-LED used during the day was 1.01, which was 26% higher than that of the c-LED; conversely, the M/P ratio of the HC-LED used at night was 0.27, which was 21% lower than that of the c-LED, as shown in Figure 3. While the participant was in the room, there were no restrictions on activities such as computer work, simple exercise, and reading a book inside the room, and hence, the illuminance at eye level may vary depending on the posture and/or gaze even under the same lighting environment. Therefore, as summarized in Table 1, the illuminance at eye level was measured using an illuminance spectrophotometer (CL-500A, Konica Minolta, Inc., Japan) assuming several cases.

Table 1. Illuminance Measured at Various Locations Depending on the Lighting Environment[a]

	daytime (08:00−18:00)			nighttime (18:00−00:00)		
		melanopic EDI (lx)			melanopic EDI (lx)	
	illuminance (lx)	c-LED	HC-LED	illuminance (lx)	c-LED	HC-LED
(a) center	500	361	478	190	60	44
(b) desk w/ monitor[b]	157	113	150			
(b) desk w/o monitor	124	90	118	51	16	12
(c) treadmill	359	259	343	143	45	33
(d) bed	156	112	149	64	20	15

[a]See Figure 1 for more information on measurement locations. Melanopic EDI, melanopic equivalent daylight illuminance; c-LED, conventional light-emitting diode; HC-LED, human-centric LED. [b]The luminance of the monitor was 117 cd/m^2 when the blue light filter was applied. Because the use of electronic video devices was prohibited after 18:00, nighttime illuminance at eye level was not measured.

2.5. Melatonin Assay. Melatonin was measured through collected saliva samples, as shown in Figure 1. Because melatonin is considered a "biological night" hormone,[31] the protocol was designed to allow larger numbers of salivary samples to be taken at nighttime. All participants were required to provide approximately 2 mL of saliva samples directly into an individual sterile tube at the specified time (a total of 15 time points). All samples were kept frozen at −60 °C until assayed. The concentration of salivary melatonin in this study was measured using equipment including a salivary melatonin enzyme immunoassay kit (Salimetrics, LLC., USA) and analyzed with an enzyme-linked immunosorbent assay (ELISA) and a microplate reader (VersaMax, Molecular Devices, LLC, USA). The ELISA kit had a detection limit of 0.78 to 50 pg/mL. During the sampling period, the participants were instructed to avoid caffeinated food and drinks, and the mean values of the duplicates were used for analyzing the result.

2.6. Statistical Analysis. All statistical analyses were performed using the IBM SPSS Statistic 26 program. Because the melatonin level is greatly suppressed during the daytime, the melatonin levels according to the lighting environments were only analyzed from 00:00 to 08:00 on the third day when 25% of the maximum melatonin level was exceeded. In particular, melatonin levels vary widely among individuals, and therefore, the Wilcoxon signed-rank tests, a nonparametric analysis, was performed (significant threshold was $p < 0.05$). Melatonin data were missing for a total of three subjects (two subjects in c-LED environment and one subject in HC-LED environment) at the last time point used in the analysis, but all remaining data were used. To analyze the SSS score, paired t tests were performed at two time points. Analysis results are represented as the mean ± standard error of the mean (SEM).

3. RESULTS AND DISCUSSION

The spectra for circadian rhythm and melatonin were derived from previous study.[27] It described the normalized spectra of the melanopic sensitivity function ($N_z(\lambda)$) and the photopic spectral luminous efficiency function ($V(\lambda)$). The human eye is most sensitive to light centered at a wavelength of 555 nm for photopic vision in terms of brightness, but light is much more effective when located at a wavelength of 480 nm for melatonin production.[6,7] However, the most commonly used chip wavelength range in the LED industry is 440 to 460 nm, and a white LED package generally consists of one blue chip corresponding to that wavelength range. Green and red or yellow phosphors are excited by blue light emitted from the chip. Cyan-color chips with wavelengths above 470 nm are rarely used in display and lighting applications because of their relatively low LE and low conversion efficiency to green or red phosphors. As such, it is difficult to fill the 460 to 500 nm region, and this gap is shown best at approximately 480 nm with a c-LED. Taking this into consideration, as shown in Figure 4, HC-LEDs were designed with two blue chips that

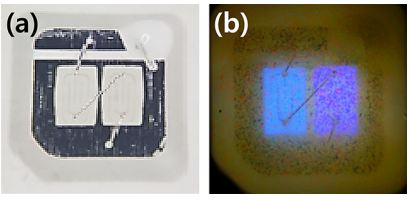

Figure 4. Microscopic images of (a) no current and (b) low current (15 mA) applied to 3.0 × 3.0 mm^2 sized human-centric (HC)-LED package with two blue chips. The peak wavelengths of the light emitted from the left and right chips were approximately 480 and 450 nm, respectively.

have been specifically customized for circadian stimulation: a conventional blue chip that emits light with a wavelength of 440 to 460 nm and a chip that emits light with a wavelength of 470 to 480 nm considering circadian rhythm. In addition, the selected LED package platform employs a size of 3.0 × 3.0 mm^2, presently the most widely used dimensions throughout the LED industry, thus ensuring flexibility in lighting module design. Optical images of the HC-LED tested at an applied current of 15 mA indicate that both chips typically emit blue light and that the color difference was due to different wavelengths. To prevent an uneven current phenomenon that may occur with the application of two chips, the package is designed with a serial circuit, which is clearly identified through a wire connected across the two blue chips.

The M/P ratio is the ratio of equivalent melanopic lux (EML) to photopic illuminance and is considered an indicator of circadian efficiency.[27] In other words, the higher the M/P ratio is, the higher the melatonin suppression at the same illuminance will be. In this regard, the spectra of daytime HC-LEDs for melatonin suppression were designed to focus on the melanopic sensitivity located at a wavelength of 480 nm

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Table 2. Performance of Daytime Human-Centric Light-Emitting Diode (HC-LED) Compared to Conventional LED (c-LED)[a]

CCT (K)	CRI (Ra)	color coordinates	Duv	M/P ratio	relative M/P ratio[b]	melanopic DER	luminous flux (lm)
3000	84.1	0.432, 0.401	−0.0005	0.65	125%	0.588	120
3500	83.3	0.408, 0.390	−0.0009	0.74	120%	0.673	124
4000	83.3	0.385, 0.380	0.0002	0.84	124%	0.761	126
5000	83.6	0.345, 0.357	0.0027	1.03	126%	0.937	124
5700	84.4	0.331, 0.343	0.0016	1.14	126%	1.032	116
6500	84.9	0.314, 0.331	0.0036	1.24	124%	1.122	109

[a]CCT, correlated-color temperature; CRI, color rendering index; Duv, delta uv; M/P ratio, melanopic/photopic ratio; DER, daylight efficacy ratio. [b]Compared to c-LEDs with the same CCT (see Table S1).

through an increase in the M/P ratio. The performance including the optical properties of the daytime HC-LED is summarized in Table 2. Figure 5a shows the CCT-dependent

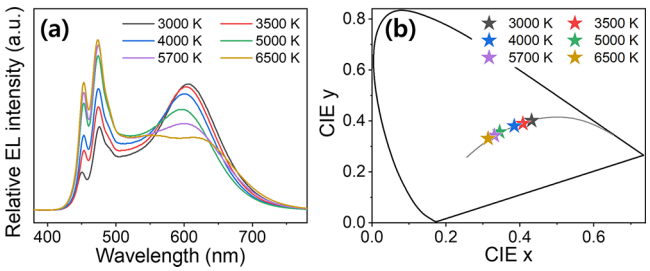

Figure 5. Optical properties of daytime HC-LED with a CCT of 3000 to 6500 K. (a) Relative electroluminescence (EL) spectra as a function of the correlated-color temperature (CCT). (b) CIE color coordinates according to CCT. The gray solid line in panel b represents the Planckian locus.

electroluminescence (EL) spectra of daytime HC-LEDs focusing and enhancing the 480 nm region for melatonin suppression. The reason for the different blue peak intensities is that the color coordinates of white light corresponding to each CCT are considerably different. Figure 5b shows the color coordinates of the daytime HC-LEDs for melatonin suppression. It can be seen that the color coordinates of the LEDs with a CCT of 3000 to 6500 K were very close to the Planckian locus. Specifically, the Duv values for these six types of LEDs are extremely low, ranging from −0.0009 to 0.0036. In addition, it was confirmed that the M/P ratio of the daytime HC-LEDs was improved by 20 to 26% compared to that of c-LEDs having the same CCT and similar structure (Figure S1). As a result, these HCL spectra can facilitate daytime melatonin suppression. Meanwhile, HC-LEDs were designed based on the M/P ratio, but according to the CIE standard newly established in 2018, this ratio can be replaced by the melanopic daylight efficacy ratio (DER).[32] In brief, the melanopic DER is expressed as the ratio of melanopic equivalent daylight illuminance (EDI) to photopic illuminance, and the melanopic EDI is a quantitative expression of nonvisual effects by ipRGC based on illuminant D65. Although the spectrum used in the EML ($N_z(\lambda)$) and the spectrum used in the melanopic EDI (melanopic action spectrum; $s_{mel}(\lambda)$) are not different, the M/P ratio and melanopic DER have slightly different values due to different criteria. For example, the M/P ratio of the daytime HC-LED with a CCT of 5000 K was 1.01, whereas the melanopic DER was 0.937; this means that the nonvisual effects on humans is 93.7% relative to illuminance D65 with a CCT of 6500 K. As the CCT increased, the proportion of blue light constituting the white light also increased, and thus the melanopic DER also increased. The luminous flux (LF) values were recorded from 109 to 126 lm, which are sufficient for indoor lighting depending on the CCT at an applied current of 150 mA.

The aforementioned daytime HC-LED packages were enhanced with a peak intensity of 480 nm for melatonin suppression. However, for the spectrum suitable for the night, the lower intensity in the 480 nm wavelength region is better in terms of melatonin secretion and circadian rhythm. Exposure to bright light at nighttime, particularly high-intensity light with a wavelength of 480 nm, can lower melatonin levels, resulting in poor sleep quality.[33] For this purpose, unlike the daytime HC-LED with an enhanced peak in the 480 nm wavelength region, a nighttime HC-LED with a reduced peak in the same wavelength region was also developed. The performance, including the optical properties of the nighttime HC-LED, is summarized in Table 3. Figure 6a shows the EL spectra of the nighttime HC-LEDs with a CCT of 1800 to 4000 K prepared for melatonin secretion. In the case of the nighttime HC-LED, the peak intensity in a wavelength region of 480 nm was reduced by using a different phosphor with a narrow full width at half-maximum (fwhm) of 50 nm instead of the phosphor with a FHWM of 100 nm used in the conventional white LED for lighting. Similar to the CCT of

Table 3. Performance of Nighttime HC-LED Compared to c-LED[a]

CCT (K)	CRI (Ra)	color coordinates	Duv	M/P ratio	relative M/P ratio[b]	melanopic DER	luminous flux (lm)
1800	84.0	0.542, 0.411	0.0009	0.21	74%	0.188	79.7
2200	84.0	0.502, 0.416	0.0002	0.29	79%	0.260	94.4
2700	84.0	0.458, 0.410	−0.0001	0.39	85%	0.350	109
3000	84.0	0.434, 0.403	0.0000	0.44	85%	0.400	122
3500	83.8	0.407, 0.392	0.0002	0.52	84%	0.471	127
4000	81.9	0.382, 0.380	0.0011	0.59	87%	0.536	118

[a]CCT, correlated-color temperature; CRI, color rendering index; Duv, delta uv; M/P ratio, melanopic/photopic ratio; DER, daylight efficacy ratio. [b]Compared to c-LEDs with the same CCT (see Table S1).

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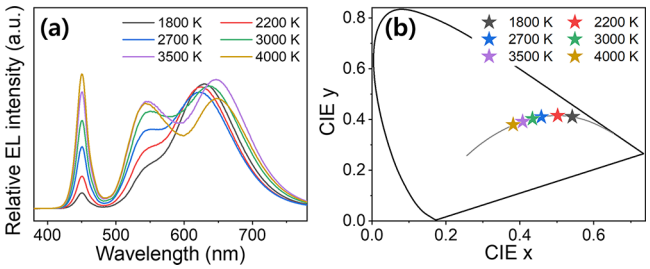

Figure 6. Optical properties of nighttime HC-LED with a CCT of 3000 to 6500 K. (a) Relative EL spectra as a function of CCT. (b) CIE color coordinates according to CCT. The gray solid line in panel b represents the Planckian locus.

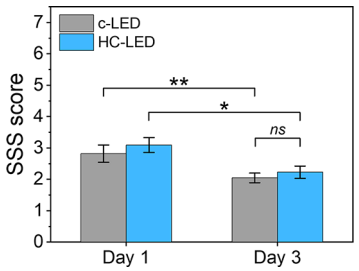

Figure 7. Stanford Sleep Scale (SSS) under c- and HC-LED lighting environments. All data represent mean ± standard error of the mean (SEM). *p < 0.05, **p < 0.01, and *ns* = not significant.

the daytime HC-LED series, it can be seen that the CCT values of nighttime HC-LEDs were very close to the Planckian locus, as shown in Figure 6b. The Duv values of nighttime HC-LEDs ranged from −0.0001 to 0.0011, which is a smaller range than that of the daytime HC-LEDs. In terms of the M/P ratio, nighttime HC-LEDs had 13 to 26% lower values depending on the CCT compared to c-LEDs due to the reduced intensity in a wavelength region of 480 nm (Figure S2). In addition, the melanopic DER values of the nighttime HC-LED were as low as 0.188 to 0.536 depending on the CCT. This means that the nonvisual effects caused by light are less compared to the c-LED having an identical CCT, and the nonvisual effects caused by light can be similar even if an HC-LED having a higher CCT is used. Meanwhile, the LF values were 79.7 to 127 lm depending on the CCT under the identical driving condition as the daytime HC-LEDs. The LF was relatively low, especially for the HC-LED with a low CCT of 1800 K, but this is a natural consequence of the $V(\lambda)$ with a peak wavelength of 555 nm and is acceptable for nocturnal circadian rhythm. Consequently, HC-LEDs with improved diurnal melatonin suppression and nocturnal melatonin secretion effects compared to c-LEDs were developed in consideration of circadian rhythm without a perceived color difference.

To establish a healthy and regular circadian rhythm, blue light exposure should increase during the daytime and decrease at nighttime. Various chip and phosphor technologies can be used in the creation of appropriate light for the daily cycle at different wavelengths. As for daytime and nighttime HC-LEDs, we confirmed that the indices representing the performance of melatonin suppression and secretion were much higher than those of c-LED lighting at the package level. To confirm that this performance can be realized in real life conditions, a verification study of the HC-LED with controlled intensity in a wavelength region of 480 nm was conducted by monitoring melatonin levels over time. Because two versions of the HC-LEDs were developed, one for daytime and another for nighttime, both versions were used during the 50 h human melatonin validation study. Therefore, it can be assumed that participants placed in the HC-LED lighting environment will have faster suppressed melatonin in the morning and more melatonin secreted at nighttime. Although melatonin is not secreted during daytime regardless of the presence or absence light, it has been reported that using blue-enriched white light during the daytime can improve workability by improving subjective alertness and drowsiness.[34,35]

To evaluate the subjective drowsiness of the participants, we administered the SSS self-questionnaires in the lighting environment. As shown in Figure 7, the first SSS evaluations in the c- and HC-LED lighting environments that were carried out 1 h after admission yielded results of 2.8 ± 0.3 and 3.1 ± 0.2, respectively. The SSS scores at this point were considered to be the score for the habitual state of the participants as they were hardly affected by the laboratory lighting. Meanwhile, the second SSS evaluations were performed 48 h after the first SSS evaluation, and values of 2.0 ± 0.2 in the c-LED lighting environment and 2.2 ± 0.2 in the HC-LED lighting environment were recorded. The second SSS score decreased significantly compared to the first SSS score (p = 0.004 in c-LED and p = 0.013 in HC-LED), which appears to be because all participants followed a defined study protocol. However, on the third day of admission, the difference in the SSS scores according to the lighting environment was not significant (p = 0.492). This appears to be because subjective drowsiness was evaluated at the time of the questionnaire, and the results may differ if subjective drowsiness is evaluated at various time points.

To evaluate the LED spectra effect on melatonin secretion, 15 salivary samples were collected during a 50 h protocol. There are three available methods for analyzing melatonin level: using blood, urine, or saliva.[36] Blood can be sampled frequently for analysis, regardless of sleep disturbance. However, its invasive nature and vein loss or collapse in some participants are possible drawbacks of using blood samples obtained via intravenous catheters. For these reasons, plasma sampling tends not to be strongly proposed for routine clinical studies. Therefore, in this study, salivary samples were used to analyze the melatonin level. Although salivary melatonin is known to be one-third as accurate as plasma melatonin, it is relatively simper to obtain and consistent.[37] In this study, the participants were instructed to go to sleep from 0:00, but they had to provide saliva samples every hour until 3:00. In other words, there were three sleep interruptions, and sample collection was not conducted after this time because the sleep disturbances were expected to be severe. Their sleep was partially disturbed, but nonetheless, under both c- and HC-LED lighting, the participants showed a well-developed circadian rhythm that suppressed melatonin during the daytime and increased secretion of melatonin at nighttime (Figure S3). Typically, melatonin level analyses are performed after dim light melatonin onset (DLMO), when melatonin is abundantly secreted. However, in this study, because there was no dim light phase, it was not possible to confirm the exact DLMO, and thus, the melatonin analysis was performed assuming a time point after DLMO. In other words, only data above 25% of the maximum melatonin levels were used to analyze differences in melatonin levels between lighting environments. The Wilcoxon signed-rank test results over

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time for c- and HC-LED lighting environments are summarized in Table S3. The melatonin levels from 00:00 to 03:00 on the third day were higher in the HC-LED lighting environment than in the c-LED lighting environment, as shown in Figure 8. However, the differences were not

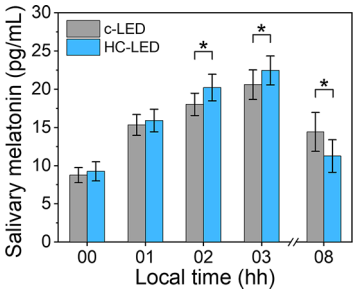

Figure 8. Melatonin level profiles obtained from salivary samples under c- and HC-LED. All data represent the mean ± standard error of the mean (SEM). *$p < 0.05$.

significant at 00:00 and 01:00 ($p > 0.05$). As the night progressed, there was a clear difference in melatonin levels, depending on the lighting environment. At 02:00, the average melatonin level increased by 2.199 pg/mL in the HC-LED lighting environment, which increased by 12.2% compared to the c-LED lighting environment ($p = 0.039$). In addition, even after an additional hour, the level was, on average, 1.864 pg/mL higher in the HC-LED lighting environment ($p = 0.042$). This indicates that the HC-LED lighting environment with a regulated wavelength of 480 nm can be more favorable for nocturnal melatonin secretion than the c-LED lighting environment. As documented in many previous studies, light-induced melatonin control is not new; however, an obvious difference between the protocol used in the previous studies related to circadian rhythm such as research on melatonin and core body temperature (CBT), the CR is performed in a semirecumbent posture under a dim light condition for at least 24 h to minimize external influences.[1−3,38−40] Instead of this CR phase, the present study set up an acclimation phase for approximately 1 day under the same light environment as the specified protocol. Nevertheless, the significant difference in melatonin levels according to the lighting environment shows that melatonin can be controlled by indoor lighting in a regular and habitual routine. Interestingly, the melatonin level was reversed before and after waking up according to the lighting environment. Immediately after waking up, the melatonin level in the HC-LED lighting environment was 3.156 pg/mL lower than that in the c-LED lighting environment, representing a 21.9% decrease compared to that in the c-LED lighting environment ($p = 0.025$). In the case of circadian rhythm phase shifts, data measured under dim light conditions are required for an accurate evaluation. In this regard, the protocol used in this study may not be suitable for identifying phase shifts. In addition, because of the complex light conditions (daytime and nighttime) included in a 50 h set, further research should be conducted to determine at which time of day the light environment has a greater effect on melatonin levels and secretion time. Nonetheless, given the nature of melatonin reaching its peak concentration between 01:00 and 04:00,[41] it can be inferred that the melatonin phase was advanced in participants placed in the HC-LED lighting environment.

Many previous studies have demonstrated the effects of wavelength and intensity of lighting on melatonin secretion.[42−45] A decrease in melatonin levels during the daytime could translate into increased vitality and work efficiency, and a nighttime increase in melatonin could enhance bodily relaxation and improve sleep quality.[34,46,47] To discuss the disturbance of circadian rhythm, not only the wavelength of light exposed at night but also the light intensity must be considered. In this case, the light intensity at eye level, i.e. vertical illuminance, is considered more important.[48] Rea et al.[49] proposed a melatonin suppression response function by light, called circadian stimulus (CS). Assuming that the participants were reading a book while obliquely leaning on a bed, the CS values of daytime c- and HC-LED lighting environments were 0.207 and 0.242, respectively, and thus, the CS value was 16.9% higher for the HC-LED than for the c-LED. In addition, in the case of the nighttime lighting environment, the CS value of the HC-LED lighting environment (0.036) was 23.4% lower than that of the c-LED lighting environment (0.047). These results are reasonable because the M/P ratios of daytime and nighttime HC-LEDs were designed differently compared with the c-LEDs. Therefore, it is anticipated that use of the developed HC-LED would help maintain a healthy circadian rhythm by further suppressing melatonin during the daytime and increasing melatonin secretion at nighttime.[50−53] However, in the 50 h protocol, the participants were not restricted in their behavior, and thus, the vertical illuminance and CS value could vary depending on their position, gaze, and posture. In addition, the vertical illuminance varies greatly depending on the characteristics of the room, such as the size of the room, the reflectance of the wall, and the location of the lighting. In this regard, a measurement method to quantify the efficiency of a luminaire to reach a certain level of CS based on a standard observer has been proposed.[54] Students or office workers who spend most of their day indoors are more exposed to artificial lighting than natural light, and thus, this test procedure is anticipated to further facilitate the design of indoor lighting to manage circadian rhythm. In particular, the corneal blue light transmittance of adolescents is higher than that of adults, and this should be considered in the design of indoor lighting.[55] Consequently, for a healthy daily life with an environment of abundant exposure to artificial light, indoor lighting should be designed with an appropriate wavelength and intensity, considering who will use it and when.

Meanwhile, our HC-LEDs were developed for indoor lighting, but the concept of using two chips emitting blue light of two different wavelengths can be applied to the display field as well. Most displays, including smartphones, televisions, and monitors, support a mode for blocking blue light at night (BLAN), but there is no mode that can quickly suppress melatonin by enhancing blue light during the daytime. For this, the nighttime HC-LED concept should be considered to minimize nocturnal melatonin suppression. The BLAN blocking mode is mostly achieved by reducing the intensity of blue light with a wavelength of 450 nm, which is mostly used in displays, resulting in a decrease in the CCT of white light due to the low blue light ratio. However, if blue lighting with a wavelength of 480 nm can be controlled, an identical effect can be obtained even at a relatively high CCT. Of course, there are aspects that should be considered first for the display performance, such as resolution, color gamut, and luminance; nevertheless, these attempts to apply HCL to the display can

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be sufficiently made from the perspective of the user's circadian rhythm. Although further studies on circadian rhythm and artificial light sources are needed, for the human circadian rhythm, there is a need for universal use of HCL, which is scalable to more fields, from daytime/nighttime indoor lighting to display applications.

4. CONCLUSIONS

HC-LEDs were designed to enhance or reduce the melanopic curve area close to 480 nm based on light exposure time periods. As a result of testing melatonin levels in 22 Korean male participants, it was found that the HCL environment had a greater effect on melatonin secretion and suppression, supporting our hypothesis. Although the study protocol should be discussed in various aspects, light-induced melatonin control appears to be sufficiently effective even for a representative day in an HCL environment. The HC-LED, which is expected to improve the circadian rhythm by controlling the wavelength band of light directly related to melatonin, will be a useful item for maintaining a healthy circadian rhythm in modern life, where people spend more time indoors.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.3c05620.

> Performance of conventional LED, the paired *t* test results for SSS questionnaires and the Wilcoxon signed-rank test results for melatonin levels, and the melatonin profiles over time and lighting environment (PDF)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. Y.J.E. performed the measurement and analyzed the measured data. S.-w.C. designed the LED package. C.K. and S.L. performed the measurement. C.Y. fabricated the LED. D.H.K. assisted to design the experimental protocol. C.K. supervised and contributed to design the experimental protocol. Y.R.D. conceived of the project, led supervision of the work.

Notes

The authors declare no competing financial interest.

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