COMPARISON OF MELATONIN PHOTODEGRADATION BETWEEN SUNLIGHT AND UV IRRADIATION

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Abstract. Melatonin is synthesized mainly in the pineal gland, retina, digestive tract, and skin. This hormone is widely prescribed for therapeutic applications such as treating circadian rhythm, intercontinental flight dysrhythmia (jet lag syndrome), and sleep disorders. As a result of the COVID-19 pandemic, the consumption of this hormone was increased up to 300% in doses higher than 5 mg day because it was used to treat insomnia and as an adjunct to treat SARS-CoV-2. Therefore, this hormone is expected to be present in surface water bodies as a pollutant. Although it is reported that melatonin can be photolabile, its photochemistry has not been exhaustively studied. For this reason, the photodegradation of melatonin in solution was evaluated in this work. Solutions of 20 and 500 µM of melatonin dissolved in water were exposed to sunlight and UVA irradiation, and the degradation was monitored by spectrophotometry and total organic carbon.
Key words: *melatonin, photodegradation, spectrophotometry, adjunct to treat SARS-CoV-2.*

INTRODUCTION

The 2030 Agenda for Sustainable Development was ratified by the United Nations Organization member states in 2015. The 2030 Agenda is a plan of action for people, the environment, and prosperity. This Agenda has 17 Sustainable Development Goals (SDGs) and lays out a strategy for achieving these goals over 15 years. Goal six of the 2030 Agenda consists of "clean water and sanitation," as the United Nations Organization reports that in 2015, 4,5 billion people lacked safely managed sanitation services, and 2,3 billion lacked even basic sanitation. Therefore, it is necessary to develop viable protocols to remove pollutants present in water, including emerging pollutants. Emerging pollutants (EC) are characterized by little or no monitoring and regulation at the national or international level because they are substances for which there is a lack of information on their occurrence, concentration, and risk to health [1]. Pharmaceuticals are one class of this type of pollutant that is of particular concern because they are introduced into water bodies mainly through the discharge of wastewater and effluent, as well as direct emissions from production sites and improper disposal of excess pharmaceuticals in households. As a result, pharmaceuticals are often not completely removed in wastewater treatment plants and are released into receiving waters [2].

Melatonin (MLT), a neuroendocrine hormone that controls the circadian cycle and is used to treat insomnia [3], has seen a surge in use both before and during the COVID-19 pandemic because of the sleep problems caused by the alarming scenario unfolding around the world. In addition, MLT has been suggested as an adjuvant in the treatment of COVID-19 in its many stages, as a prophylactic measure, as therapy in intensive care units, and to enhance the effectiveness of vaccinations [4]. MLT is available in tablets and capsules for human consumption and is sold without a prescription in many countries, even over the counter in health food stores [5].

As a result, Li et al. (2022) [6] reported an increase in the use of MLT of up to 300% (comparing the years 1999 and 2018), even at doses higher than 5 mg day [1]; the increase in use was 28% in the US adult population. About the child population, which was at home as a means of protection during the pandemic, it was reported that there was an increase in accidental ingestion of MLT, causing the death of two children under two years of age and requiring mechanical ventilation in the other five cases. In Ontario, Canada, melatonin supplements that contain up to 478% more melatonin than stated on the label are marketed. 26% of those products contain serotonin, a product of MLT dysfunction, in clinically significant doses, as it is a controlled medication prescribed to maintain emotional balance and combat depression [7].

Although the consumption of melatonin is considered safe, adverse effects such as headache, insomnia, rash, stomach upset, and nightmares have been reported. However, other authors report that 150 to 450 ngL-1 of MLT consumption can suppress testosterone production, decrease semen quality, and affect sexual activity and reproduction in animals and humans [8,9].

Therefore, there is a great need to search for methods to treat and remove this pollutant. One alternative is represented by photolysis, a chemical process that breaks chemical bonds because of the transfer of light energy (direct photolysis) or radiation energy (indirect photolysis) to these bonds [10].

Therefore, in this work, the evaluation of the photodegradation of melatonin using sunlight and a 365 nm UV lamp is reported.

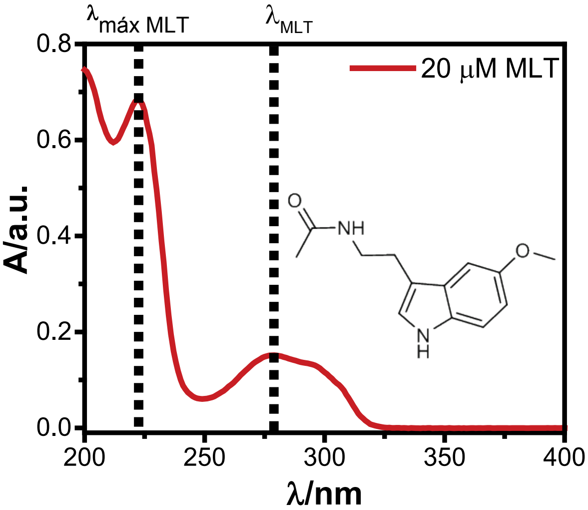

Figure 1. UV-Vis spectra of MLT 20 μM in aqueous medium

METHODOLOGY

Melatonin (CAS: 73-31-4) and pure ethyl alcohol (CAS: 64-17-5) were purchased from Sigma Aldrich. Solutions of melatonin were prepared with deionized water, and the minimum amount of pure ethyl alcohol was required to solubilize melatonin. In this case, 20 and 500 μM of melatonin solutions were evaluated in photolysis experiments by sunlight and ultraviolet (365 nm = UVA) irradiation.

For the sunlight-irradiated solutions, 40 mL of each MLT concentration was placed in a glass bottle to reach the sunlight. Each solution was monitored by UV-Vis spectrophotometry (CARY 50BIO UV-Visible Spectrophotometer) at different exposure times, and the total organic carbon (Total Organic Carbon Analyzer Shimadzu TOC-LCSN) allowed to monitor the percentage of mineralization of the sample.

On the other hand, the lamp used during ultraviolet irradiation was a UVP Blak-Ray XX-15BLB (15 watts-365 nm (UVA)), using 8 mL of each MLT solution (20 or 500 μM). In this case, these samples were placed in beakers and they were mechanically stirred during the experiment. As with the sunlight-exposed samples, these samples were monitored by UV-Vis spectrophotometry and total organic carbon analysis.

RESULTS AND DISCUSSION

Figure 1 shows the characteristic spectrum of a 20 M MLT solution in an aqueous medium. It can be observed that MLT has two bands, one at $\lambda_{máx}$=222 nm and the other at λ=278 nm.

Photolysis by sunlight irradiation. In the UV-Vis spectra shown in Figure 2a and Figure 2b it is possible to observe the gradual shift of the $\lambda_{máx}$ of the MLT, located at 222 nm, towards 232 nm. For the absorption band λ= 278 nm, the observed shift is towards 269 nm, and it is also possible to observe an absorption band in the range of 300 to 350 nm, whose intensity value increases with the hours of exposure to sunlight. Furthermore, in these figures, isosbestic points at 272 and 310 nm can be observed, which indicates the formation of melatonin oxidation products [11]. This behavior becomes even more obvious when looking at Figure 2c and Figure 2d, which show the comparison of the UV-Vis spectra of MLT solutions c) 20 μM and d) 500 μM before (red curve) and after 125 h (blue curve) of exposure to sunlight.

According to [12], Figure 3 shows the possible photodegradation pathway of MLT when exposed to sunlight.

Regarding total organic carbon analysis, the percentage of mineralization obtained was ~44% for both solutions.

Photolysis by UV irradiation. In the UV-Vis spectra shown in Figure 4a and Figure 4b, it is possible to observe that the $\lambda_{máx}$ of the MLT, located at 222 nm, does not undergo any change when the solution evaluated is 20 μM MLT, contrary to the case of 500 μM MLT solution, where a slight decrease in absorbance is observed.

In both solutions, it is possible to observe the formation of new absorption bands at 270 and 350 nm, indicating the presence of degradation products, and these bands are consistent with those observed in the degradation of melatonin by sunlight.

Figure 5 shows the change in the total organic carbon normalized to the initial value with respect to the UV irradiation exposure for the two solution concentrations of MLT evaluated. After 8 hours of treatment, the percentage of mineralization was 75% for the 20 μM of MLT solution, while in the case of the 500 μM solution, the removal percentage was 66%.

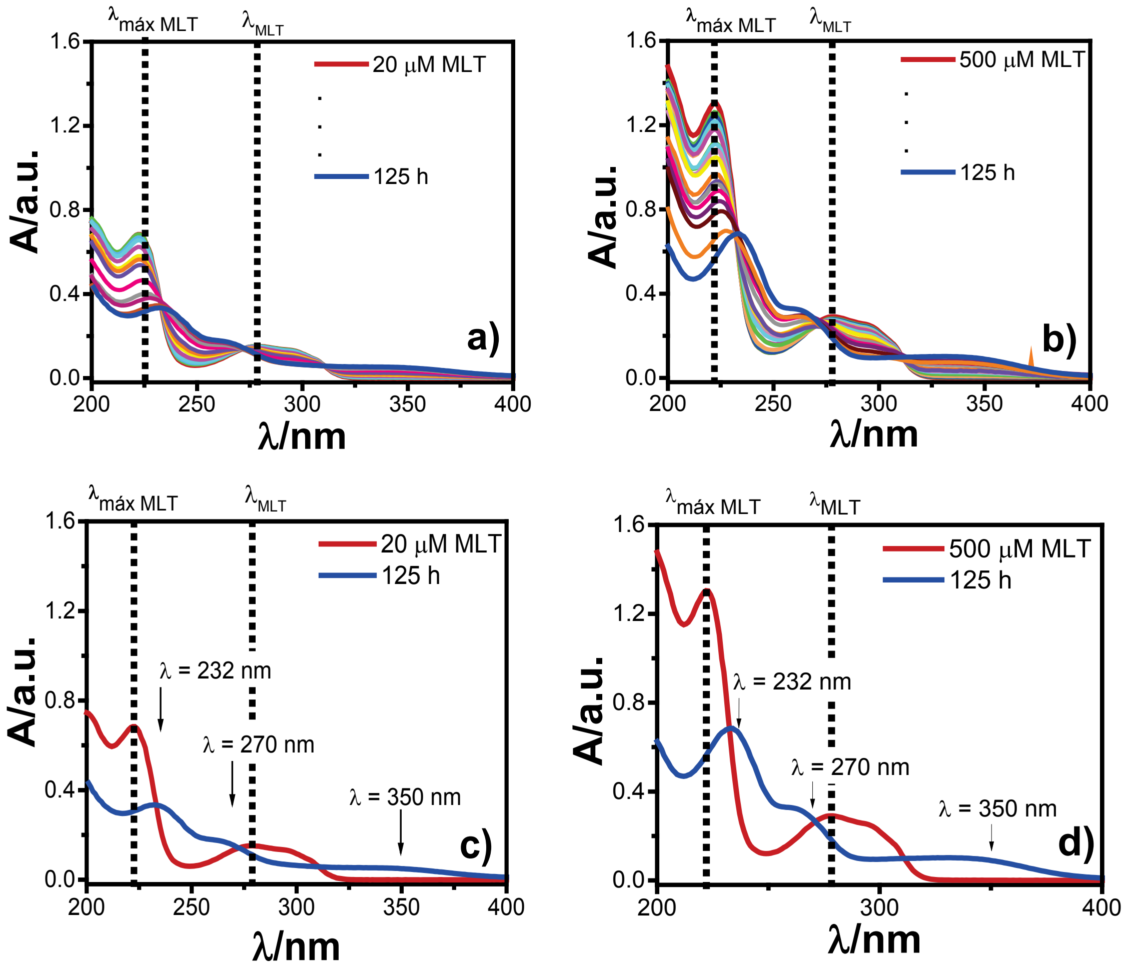

Figure 2. UV-Vis spectra of MLT a) 20 M and b) 500 M concentrations at different times of sunlight exposure. Comparison of UV-Vis spectra of MLT c) 20 M and d) 500 M concentrations before (red curve) and after 125 h of sunlight exposure (blue curve)

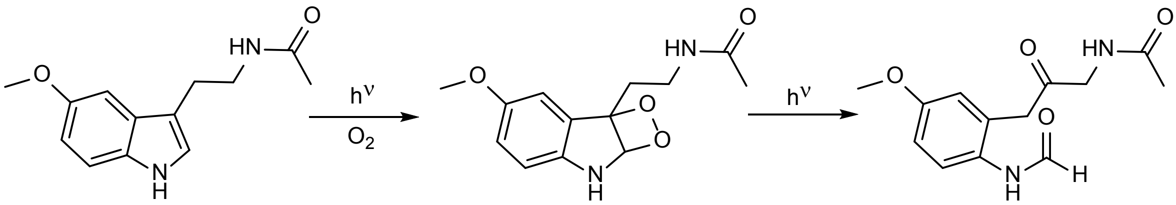

Figure 3. Melatonin degradation photoproduct, according to [12].

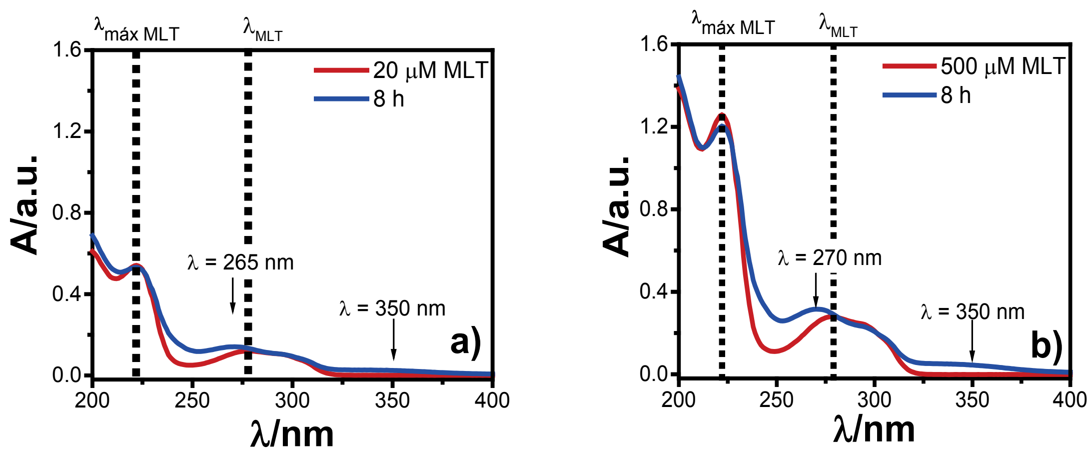

Figure 4. Comparison of UV-Vis spectra of MLT a) 20 M and b) 500 M concentration, irradiated with UV light (365 nm) during 480 min

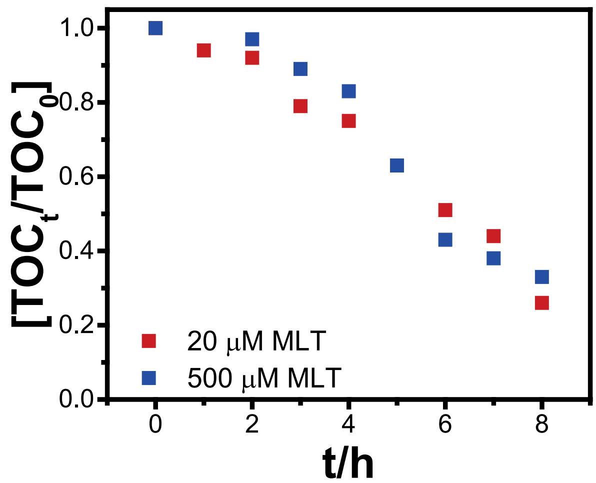

Figure 5. [TOCt/TOC$_0$] vs. UV irradiation time exposure of 20µM and 500 µM of MLT concentration

CONCLUSIONS

UV-Vis spectrophotometry and TOC techniques were used to analyze the degradation of 20 µM and 500 µM of MLT exposed to sunlight and UV irradiation. It was observed that two absorption bands were formed at 270 nm and 350 nm as a result of MLT photodegradation, being more visible during sunlight irradiation. However, TOC analysis only showed 44% of mineralization abatement in both MLT concentrations at the end of 125 h of sunlight irradiation. On the other hand, the TOC abatement using UV irradiation showed a decrease of ~70% in both MLT concentrations only in 8 h of exposure. These results suggest that UVA is more effective in photodegrading MLT in water than sunlight irradiation. However, it is necessary to analyze the subproducts using chromatography techniques.

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СРАВНЕНИЕ ФОТОДЕГРАДАЦИИ МЕЛАТОНИНА ПОД ВОЗДЕЙСТВИЕМ СОЛНЕЧНОГО СВЕТА И УЛЬТРАФИОЛЕТОВОГО ИЗЛУЧЕНИЯ

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Аннотация. Мелатонин синтезируется главным образом в шишковидной железе, сетчатке, пищеварительном тракте и коже. Этот гормон широко назначают в терапевтических целях, таких как лечение циркадных ритмов, аритмии при межконтинентальных перелетах (синдром смены часовых поясов) и нарушений сна. В результате пандемии COVID-19 потребление этого гормона было увеличено до 300% в дозах выше 5 мг в день, поскольку его использовали для лечения бессонницы и в качестве вспомогательного средства при лечении SARS-CoV-2. Таким образом, ожидается, что этот гормон будет присутствовать в поверхностных водоемах в качестве загрязнителя. Хотя сообщается, что мелатонин может быть фотолабилен, его фотохимия до конца не изучена. По этой причине в данной работе оценивалась фотодеградация мелатонина в растворе. Растворы мелатонина с концентрацией 20 и 500 мкМ, растворенные в воде, подвергали воздействию солнечного света и ультрафиолетового излучения, а деградацию контролировали с помощью спектрофотометрии и общего органического углерода.

Ключевые слова: *мелатонин, фотодеградация, спектрофотометрия, средство лечения SARS-CoV-2.*