

EDITORIAL

Pharmacology without drugs



Jesús Pintor*

Dep. Biochemistry, Fac. Optometry, Universidad Complutense de Madrid, C/ Arcos de Jalon 118, 28037 Madrid, Spain

Available online 1 August 2018

Pharmacology is moving forward by using new and more advanced techniques. Targets such as receptors, enzymes and nucleic acids are stimulated or inhibited by means of a plethora of compounds such as agonists, antagonists, substrates, inhibitors, etc. in order to get the desired effect. Therefore, a common practice in pharmacology is the use of selective substances to produce an effect in most of the cases with therapeutic purposes.¹

Nonetheless, is it possible to obtain a pharmacological effect and a subsequent physiological or therapeutic effect without using an agonist or an antagonist, i.e., without applying a drug?

Receptor-drug interaction is necessary to obtain a given effect; nevertheless, in some cases, instead of using a chemical messenger or drug it is possible to play with something that surrounds us: light.

Light predates any living being on earth and is therefore, probably, the most powerful physical agent that has conditioned the evolution on our planet.² Accordingly, living organisms have developed systems to detect light and, of course, to take advantage of it. Moreover, most living organisms have an internal mechanism which coordinates many physiological processes depending on the presence or

E-mail address: jpintor@ucm.es

absence of light. Thus, the development of a structure to use light, like the eye, is present in very primitive organisms and the most evolved ones alike.³ The existence of an eye is indeed crucial for the survival of almost all species. However, light can be used for more than just forming images.

The discovery of melanopsin, a receptor protein that can capture light without being involved in the formation of images, opened a new interesting perspective. Its discovery has explained how most organisms can control and regulate diurnal and nocturnal processes, in what are called circadian rhythms.⁴ Melanopsin was initially described to be present in a subset of retinal ganglion cells termed *intrinsic photosensitive retinal ganglion cells*. These cells connect to the suprachiasmatic nucleus and from there towards the pineal gland where melatonin is synthesised when light is absent.⁵

Recently, it has been possible to demonstrate the presence of melanopsin in the human lens, particularly in its epithelium. Interestingly, the stimulation of this protein with white light, in particular by the blue component of white light (λ 460–485 nm), did inhibit the local synthesis of melatonin in the lens. On the contrary, the lack of light, or light with wavelengths distant from blue colour, produced a marked stimulation of melatonin production by increasing the expression of one of the key enzymes of its synthesis, aralkylamine N-acetyltransferase (AANAT). Altogether, this indicates that modulating light properties, permitting the stimulation or not of melanopsin, can result in pharmacological responses without the use of any drug.⁶

https://doi.org/10.1016/j.optom.2018.06.002

1888-4296/© 2018 Spanish General Council of Optometry. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).



^{*} Correspondence to: Department of Biochemistry, Faculty of Optics and Optometry, Complutense University of Madrid, C/ Arcos de Jalón 118, E-28037 Madrid, Spain.



Fig. 1 Light-mediated effect on the lens. (A) White light, and in particular its blue component, stimulates the melanopsin receptor blocking the local synthesis of melatonin in the lens. (B) When a filter eliminating blue light component (λ 460–485 nm) is used, melanopsin is not stimulated and the local synthesis of melatonin in the human lens epithelium occurs. Since melatonin is released to the aqueous humour, this substance can act on melatonin receptors present in the ciliary body reducing intraocular pressure.

Is it possible to regulate the activity of melanopsin and therefore its elicited effects? It certainly is. Indeed, the use of filters limiting the presence of the blue component of sunlight produces marked effects on melatonin synthesis. In this sense, the application of such filters to experimental animals has permitted the observation of a gradual increase of melatonin levels in their aqueous humour. Moreover, such elevation in melatonin concentration has a strong effect on intraocular pressure (IOP), reducing this physiological parameter (Fig. 1). This means that by using filters, and avoiding the stimulation of melanopsin, an elevation of melatonin occurs and a concomitant reduction in IOP happens. This might be of special relevance for those patients suffering from ocular hypertension and glaucoma, since they may benefit from an extra IOP reduction complimentary to the pharmacological treatment they are receiving.

Also, it could be the case that when melanopsin is not activated the resulting production of melatonin in the lens could help to stop the development of cataracts. Melatonin has been described as an antioxidant molecule itself, without the action of any receptor or enzyme. Therefore, the use of a filter for blue light in spectacles or contact lenses could be of interest to stop cataract progression or to delay its onset.^{7,8}

Since the eye is characterized by many transparent media, all of which allow light through, it is very probable that if melanopsin is present in other ocular structures, it may regulate several crucial eye physiological processes. It is only a matter of time to determine where melanopsin is present in the eye to start modulating light in order to achieve positive therapeutic actions on ocular parts such as the cornea or the ciliary body.

Obtaining pharmacological effects without the use of agonists and antagonists but by means of filters and light manipulation will represent a new challenge merging pharmacologists and optometrists in order to obtain new and revolutionary treatments for ocular pathologies.

Acknowledgements

This work was supported by research grants from the Spanish Ministry of Economy and Competitivity (SAF-2013-44416-R, SAF2016-77084R) and the Ministry of Health Social Services and Equality RETICS (Grant RETICS RD16/0008/0017 and RD12/0034/0001).

References

- [1]. Christ GJ, Chen AF. The grand challenge for integrative and regenerative pharmacology. *Front Pharmacol.* 2011;2:5.
- [2]. Arbab I. The length of the day: a cosmological perspective. Prog Phys. 2009;1:8–11.
- [3]. Pleyer U, Pohlmann D. [Anatomy and immunology of the eye]. Z Rheumatol. 2017;76:656–663.
- [4]. Provencio I, Jiang G, De Grip WJ, Hayes WP, Rollag MD. Melanopsin: an opsin in melanophores, brain, and eye. Proc Natl Acad Sci U S A. 1998;95:340–345.
- [5]. Reiter RJ, Tan DX, Galano A. Melatonin: exceeding expectations. *Physiology*. 2014;29:325–333.
- [6]. Alkozi HA, Wang X, Perez de Lara MJ, Pintor J. Presence of melanopsin in human crystalline lens epithelial cells and its role in melatonin synthesis. *Exp Eye Res.* 2017;154:168–176.
- [7]. Abe M, Reiter RJ, Orhii PB, Hara M, Poeggeler B. Inhibitory effect of melatonin on cataract formation in newborn rats: evidence for an antioxidative role for melatonin. J Pineal Res. 1994;17:94–100.
- [8]. Bai J, Dong L, Song Z, et al. The role of melatonin as an antioxidant in human lens epithelial cells. *Free Radic Res.* 2013;47:635-642.