

# THE OXIDATION PRODUCTS OF MELATONIN DERIVATIVES EXHIBIT ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE INHIBITORY ACTIVITY

Zuzanna Mołęda, Zbigniew Czarnocki,

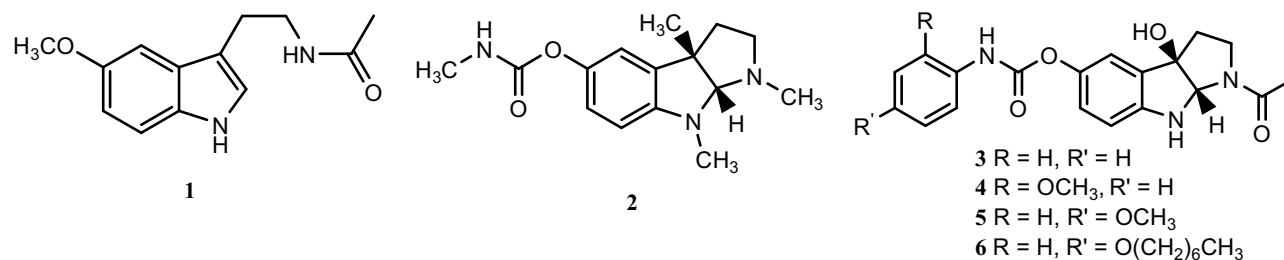
Aleksandra Siwicka, Krystyna Wojtasiewicz, Anna Zawadzka

*University of Warsaw, Faculty of Chemistry, Laboratory of Natural Products Chemistry,*

*ul. Pasteura 1, 02-093 Warsaw, Poland*

E-mail: czarnoz@chem.uw.edu.pl

It is already well documented that melatonin **1** exhibits strong antioxidant properties. It traps several reactive oxygen species including singlet oxygen, peroxy and hydroxyl radicals. Also, peroxy nitrite-induced reactions are inhibited by melatonin. The oxidation of melatonin by singlet molecular oxygen [ $O_2 (^1\Delta_g)$ ] may produce cyclic 3-hydroxymelatonin whose structure we have already studied. In this investigation we report on the synthesis of several melatonin analogues having a carbamate substituent instead of the methoxy group at 5 position of the indole ring. These compounds behave analogously to melatonin with respect to singlet oxygen and produce the corresponding cyclic 3-hydroxymelatonin analogues. The structures of the products were investigated with spectral methods and X-ray crystallography. The compounds obtained possess the 2,3,8,8a-tetrahydropyrrolo[2,3-b]indole heterocyclic system which is a structural motif characteristic of alkaloids physostigmine **2** and phenserine, that are potent acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitors used in the Alzheimer's disease treatment.



We measured the inhibitory activity of the obtained compounds against AChE and BChE from human erythrocytes and serum. In the case of the compounds having a phenylcarbamate and methoxyphenylcarbamate substituents (**3** and **5**), the inhibitory activity ( $IC_{50}$ ) ranged from  $0.252 \pm 0.033$  to  $3.804 \pm 0.581 \mu\text{M}$  [1]. Other compounds were even more active and showed rather complex interactions with the structure–activity relationship in need of further investigation.

## REFERENCES

[1] A. Siwicka *et al.*, *J. Pineal Res.* **2008**, *45*, 40.