DOCTORAL DISSERTATION ABSTRACTS

THE SYNTHESIS, STRUCTURE ELUCIDATION, ANTIMICROBIAL ACTIVITY AND QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP ANALYSIS OF SOME NOVEL 2-BENZYL-5-SUBSTITUTEDBENZOXAZOLE DERIVATIVES

Betül TEKİNER-GÜLBAŞ
Supervisor: Prof. Dr. İsmail YALÇIN, Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 06100 Tandoğan, Ankara-TURKEY
Date of examination: January 23, 2003

In this research, 23 compounds were synthesized for the first time, their in vitro antimicrobial activities were determined and their quantitative structure-activity relationships were studied.

The compounds were synthesized by condensing 2-benzyl-5-aminobenzoxazoles and/or 2-(p-chlorobenzyl)-5-aminobenzoxazoles and carboxylic acid chlorides, which were obtained by treating carboxylic acids with thionyl chloride.

The purity of the compounds was controlled by TLC and melting points were determined. Their structures were elucidated using IR, 1H-NMR and Mass analysis methods.

The antibacterial activitity of these compounds against some Gram-positive bacteria such as *Staphylococcus aureus* ATCC 25923 and *Bacillus subtilis* ATCC 6633, and Gram- negative bacteria such as *Escherichia coli* ATCC 23556 and *Pseudomonas aeruginosa* ATCC 10145, and the antifungal activity against the fungi *Candida albicans* ATCC 10231, *Candida krusei* ATCC 6258 and *Candida glabrata* were determined as the Minimum Inhibitory Concentration (MIC) values. The MIC values of the derivatives were compared to some antibacterial and antifungal drugs.

All of the compounds having MIC values as 3.12-200 *g/ml were found active against *E. coli, P. aeruginosa* as Gram-negative, *S. aureus, B. subtilis* as Gram-positive and *C. albicans, C. krusei, C. glabrata* as fungi.

The quantitative structure-activity relationships (QSAR) analysis and DFT (Discrete Fourier Transform) analysis of synthesized compounds were performed using Hansch analysis method and B3LYP/6-31G(d,p) basic set on Gaussian-98 computer program, respectively.

Key Words: Benzoxazole, benzamide, phenylacetamide, antimicrobial effect, antibacterial activity, antifungal activity, quantitative structure-activity relationships, Hansch analysis.

DOCTORAL DISSERTATION ABSTRACTS

SYNTHESIS, STRUCTURAL ANALYSIS, AND BIOLOGICAL ACTIVITY STUDIES ON ANTIOXIDANT ENZYME SYSTEM, STRUCTURE-ACTIVITY RELATIONSHIPS OF NOVEL MELATONIN DERIVATIVES

Zeynep ATEŞ-ALAGÖZ
Supervisor: Prof. Dr. Erdem BÜYÜKBİNGÖL, Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 06100 Tandoğan, Ankara-TURKEY
Date of examination: January 28, 2003

In this study, it was aimed to design and synthesize 24 1- and/or 5-substituted melatonin derivatives of which 21 of 24 are derived as novel indole compounds. Compounds bearing substituent at 5th position were synthesized in four steps while the compounds having substituent at 1st and 5th positions were synthesized in five steps.

The compounds expected to show antioxidant activity were:

1: N[2(1H-indol-3-yl)ethyl]acetamide
2: N[2(1H-indol-3-yl)ethyl]propionamide
3: N[2(1-ethyl-1H-indol-3-yl)ethyl]acetamide (New)
4: N[2(1-n-propyl-1H-indol-3-yl)ethyl]acetamide (New)
5: N[2(1-isopropyl-1H-indol-3-yl)ethyl]acetamide (New)
6: N[2(1(p-fluorobenzyl)1H-indol-3-yl)ethyl]acetamide (New)
7: N[2(1(o,p-dichloroenzyl)1H-indol-3-yl)ethyl]acetamide (New)
8: N[2(1-ethyl-1H-indol-3-yl)ethyl]propionamide (New)
9: N[2(1-n-propyl-1H-indol-3-yl)ethyl]propionamide (New)
10: N[2(1-isopropyl-1H-indol-3-yl)ethyl]propionamide (New)
11: N[2(1(p-fluorobenzyl)1H-indol-3-yl)ethyl]propionamide (New)
12: N[2(1(o,p-dichlorobenzyl)1H-indol-3-yl)ethyl]propionamide (New)
13: N[2(5-methoxy-1H-indol-3-yl)ethyl]acetamide (Melatonin)
14: N[2(5-methoxy-1H-indol-3-yl)ethyl]propionamide
15: N[2(5-methoxy-1-ethyl-1H-indol-3-yl)ethyl]acetamide (New)
16: N[2(5-methoxy-1-n-propyl-1H-indol-3-yl)ethyl]acetamide (New)
17: N[2(5-methoxy-1-isopropyl-1H-indol-3-yl)ethyl]acetamide (New)
18: N[2(5-methoxy-1(p-fluorobenzyl)1H-indol-3-yl)ethyl]acetamide (New)
19: N[2(5-methoxy-1(o,p-dichlorobenzyl)1H-indol-3-yl)ethyl]acetamide (New)
20: N[2(5-methoxy-1-ethyl-1H-indol-3-yl)ethyl]propionamide (New)
21: N[2(5-methoxy-1-n-propyl-1H-indol-3-yl)ethyl]propionamide (New)
22: N[2(5-methoxy-1-isopropyl-1H-indol-3-yl)ethyl]propionamide (New)
23: N[2(5-methoxy-1(p-fluorobenzyl)1H-indol-3-yl)ethyl]propionamide (New)
24: N[2(5-methoxy-1(o,p-dichlorobenzyl)1H-indol-3-yl)ethyl]propionamide (New)

The purity of the compounds was controlled by TLC and melting point determinations followed by the compounds fully purified by column chromatography. The compounds were elucidated by IR, NMR, and Mass spectral and elemental analysis.

Novel melatonin derivatives were screened in order to determine their inhibitory actions on the NADPH-bounded lipid peroxidation activity of microsomal mixed-function oxidase system of rat liver. It was found that compounds 3, 4, 6, 11, 18, 20, 22 and 23 showed significant inhibitory activity when compared with melatonin and antioxidant reference compound BHT (buthylhydroxytoluene).

Key Words: Melatonin, indole, lipid peroxidation, antioxidant.

DOCTORAL DISSERTATION ABSTRACTS

INVESTIGATION ON *Ferulago isaurica peşmen* AND *F. syriaca Boiss.* (UMBELLIFERAE) SPECIES

Ceyda Sibel (ERDURAK) KILIÇ
Supervisor: Prof. Dr. Maksut COŞKUN, Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 06100 Tandoğan, Ankara-TURKEY
Date of examination: September 12, 2003

The aim of this study was to compare two morphologically close species that grow naturally in Turkey: *Ferulago isaurica*, an endemic species for Turkey and *F. syriaca*, a species that has limited distribution.

For this purpose, morphological and anatomical features of the species have been investigated, and similarities and differences demonstrated with drawings and photographs.

The aerial and underground parts of both species have been analyzed for major active substance groups.

Chloroform fractions of roots of both species have been analyzed for major active substance groups. Eight compounds from *F. isaurica*, one of which is a sterol derivative, were isolated and their structures identified. All of these coumarins are furanocoumarin types. Two of them have been isolated for the first time, identified and named as maksutin and okuyamanin. From *F. syriaca* roots, five furanocoumarin derivatives were isolated and the coumarin contents of chloroform fractions of roots of both species were described.

Felamedin and prantschimgin were found to be the major coumarin components; the roots were analyzed by means of quantitative HPLC for these compounds.

The volatile oil contents of fruits and roots of both species were established and it has been shown that the species have different components.

Different extracts of aerial and underground parts and volatile oils of fruits and roots of both species were tested against some bacteria and fungi for their antibacterial and antifungal activities.

Since water extracts of the roots have been used as aphrodisiacs traditionally, this activity was also investigated and it was found that especially F. sriaca root extract has significant activity on erectile dysfunction.

Key Words: Ferulago, Umbelliferae, furanocoumarin, coumarin, felamedin, prantschimgin, aphrodisiac, HPLC.