# ANTIMICROBIAL AND ANTIOXIDANT ACTIVITY OF FERROCENE-CONTAINING PYRIMIDINE DERIVATIVES OF CURCUMIN

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## INTRODUCTION

**Although curcumin, a naturally occurring polyphenol from the rhizome of the turmeric plant, has a number of biological benefits, preclinical studies show that it cannot be used to treat diseases due to its poor bioavailability. To overcome this drawback, there is great interest in its structural modification and the synthesis of curcumin derivatives and analogues with improved bioavailability and pharmacological properties [1]. Among these analogues, the heterocyclic curcuminoids stand out, as the replacement of the β-diketo group by the rigid heterocyclic ring has led to various changes in biological activities compared to those of curcumin [2]. On the other hand, ferrocene has been shown to be an excellent candidate for the derivatization of natural products, many of which exhibit improved pharmacological properties [3]. The aim of this study was to investigate the antimicrobial and antioxidant activity of newly synthesized ferrocenylpyrimidine derivatives of curcumin (Fig. 1).**

## CHEMISTRY

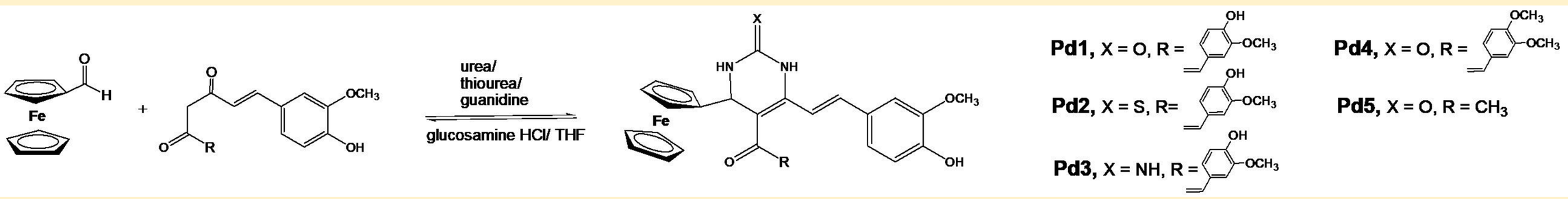


**Figure 1. Synthetic path of new ferrocene-containing pyrimidine derivatives of curcumin (Pd1-Pd5).**

## ANTIMICROBIAL ACTIVITY

**The antimicrobial activity of the target compounds was investigated against Gram-positive and Gram-negative bacteria, lactic acid bacteria, and yeasts (Fig. 2, Tab. 1).**

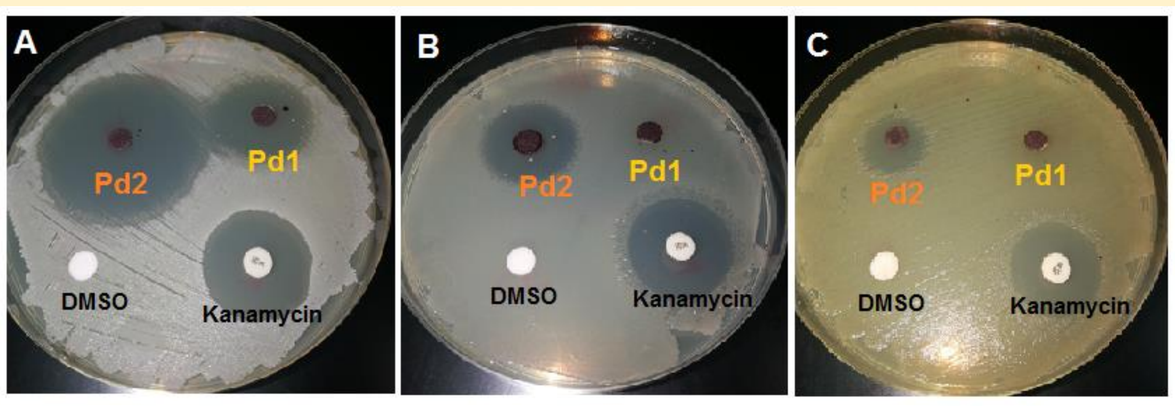


**Figure 2. Inhibition zone of compound Pd1 and Pd2 against *S. aureus* (A), *S. enterica s.* Typhimurium (B) and *E. coli* (C); (1mg/disk; Kanamycin 50 µg disk - positive control, DMSO - negative control)**

**Table 1. Growth inhibition zones of the tested microorganisms and minimum inhibitory concentrations (MIC) of the tested compounds Pd1 and Pd2.**

| | Inhibition zones (mm) | | | MIC | |
|---|---|---|---|---|---|
| Microorganisms | Pd1 | Pd2 | Kanamycin/ Nystatin | Pd1 | Pd2 |
| *S. aureus* | 25 ± 2 | 40 ± 2 | 22 ± 1 | 0,5 mM | 62,5 µM |
| *B. subtilis* | 30 ± 0 | 39 ± 1 | 15 ± 0 | 0,5 mM | 125 µM |
| *E. faecium* | 30 ± 1 | 40 ± 3 | 10 ± 0 | 1 mM | 125 µM |
| *L. monocytogenes* | 35 ± 3 | 49 ± 2 | 15 ± 1 | 1 mM | 62,5 µM |
| *P. aeruginosa* | 0 | 0 | 16 ± 0 | / | / |
| *E. coli* | 0 | 18 ± 0 | 20 ± 1 | / | 0,5 mM |
| *S. enterica s. Typhimurium* | 0 | 22 ± 1 | 22 ± 0 | / | 0,5 mM |
| *C. utilis* | 0 | 20 ± 2 | 25 ± 2 | / | > 2 mM |
| *C. albicans* | 0 | 0 | 18 ± 1 | / | / |
| *S. cerevisiae* | 0 | 0 | 18 ± 1 | / | / |

## ANTIOXIDANT ACTIVITY

**The antioxidant activity was estimated using (DPPH) and (ABTS) assays to determine the free radical scavenging ability of the compounds (Tab. 2)**

**Table 2. Antioxidant activity (DPPH and ABTS) of the ferrocene-containing pyrimidine derivates of curcumin**

| Compounds (1 mM) | DPPH (mM Trolox) | ABTS (mM Trolox) |
|---|---|---|
| Pd1 | 0.25 ± 0.01 | 1.59 ± 0.02 |
| Pd2 | 0.27 ± 0.01 | 1.42 ± 0.00 |
| Pd3 | 0.11 ± 0.02 | 0.53 ± 0.06 |
| Pd4 | 0.05 ± 0.01 | 1.43 ± 0.04 |
| Pd5 | 0.17 ± 0.01 | 1.41 ± 0.06 |
| Curcumin | 1.185 ± 0,014 | 2.23±0,03 |

## CONCLUSIONS

- **New ferrocene-containing pyrimidine derivatives of curcumin Pd1-Pd5 were prepared by the one-pot multicomponent Biginelli reaction and their structures were confirmed by FTIR, NMR and MS**
- **Compounds Pd1 and Pd2 showed strong antibacterial activity, especially Pd2 (3,4-dihydropyrimidine-2-thione derivative of curcumin), while compounds Pd3-Pd5 showed no antimicrobial activity.**
- **The minimum inhibitory concentrations (MIC) for Pd2 are in the range of 62.5 µM - 500 µM, which characterizes it as a potent antimicrobial compound whose antimicrobial activity will be further investigated.**
- **The tested compounds (1 mM) showed antioxidant activity against both DPPH and ABTS radicals. Compound Pd2 showed the highest DPPH antiradical activity, while compound Pd1 showed the highest ABTS antiradical activity.**

## LITERATURE

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## ACKNOWLEGEMENT

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