Effect of amoxicillin metabolites on the induction of resistance to amoxicillin susceptible bacterial strains

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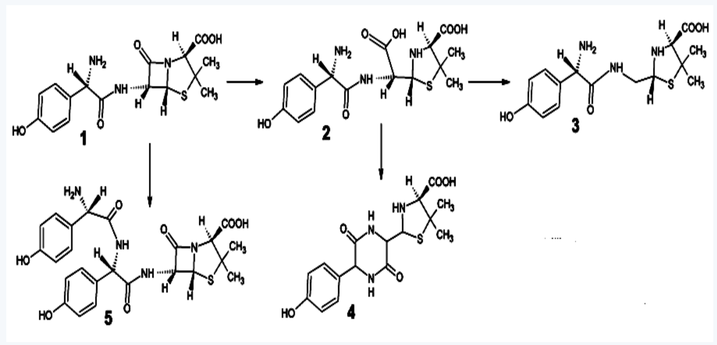
Introduction

Amoxicillin is an antibiotic utilized to treat bacterial infections in humans and animals. In the body, amoxicillin undergoes metabolism changes where metabolites remain in the tissues longer than the parent compound. The metabolites remaining in the tissues as well as those released into the environment may lead to the induction of bacterial resistance.



Pic. 1. Scheme of amoxicillin degradation: 1) amoxicillin, 2) amoxicillin acid, 3) amoxillin acid, 4) amoxicillin piperazin-2,5-dion 5) 4-hydroxyphenylglycol of moxicillin.

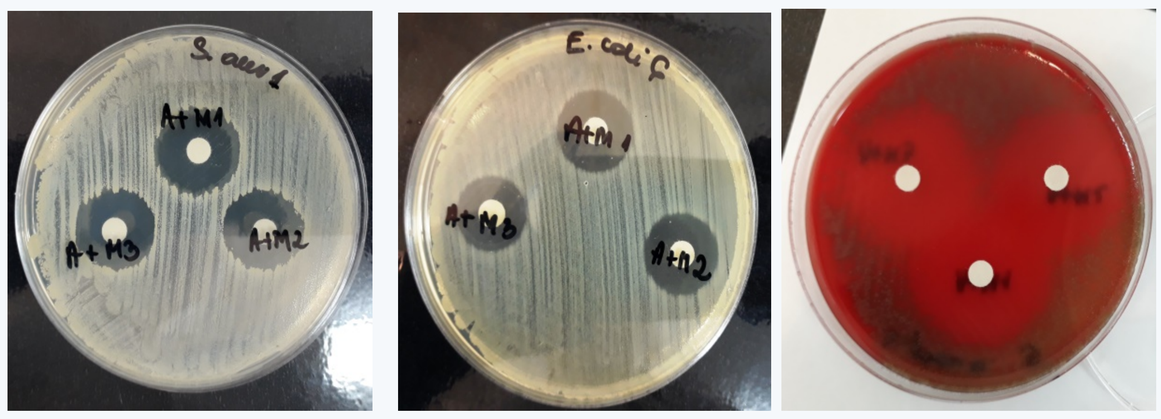
The aim of the study

The aim of this study was to examine the influence of three amoxicillin metabolites (AMA – amoxicillin acid, MONO – amoxillin acid and DIKETO – amoxicillin piperazin-2,5-dion) on antimicrobial activity of parent compound.

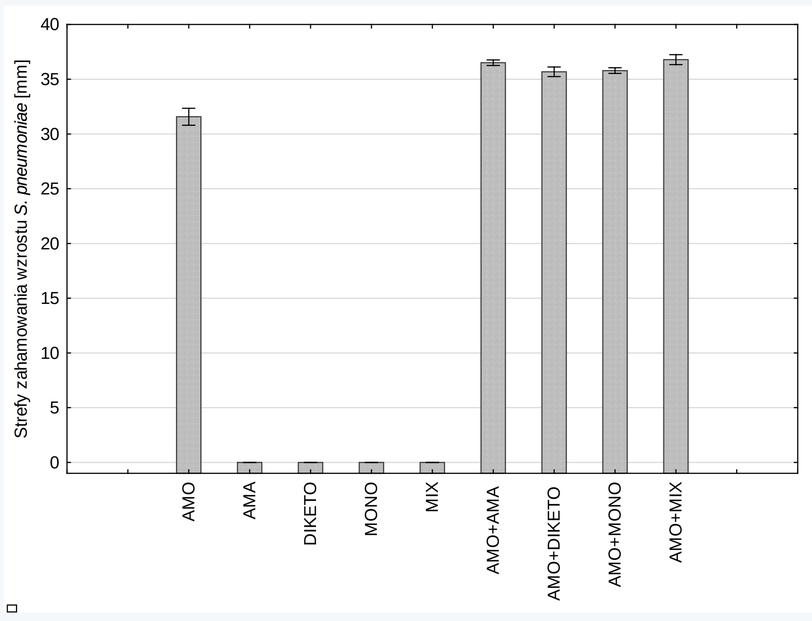
Materials and methods

The study was conducted on three microorganisms: *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 23213 and *Streptococcus pneumoniae* ATCC 49619. Bacterial suspensions with a density of 0.5 MF were seeded on solid media: Mueller-Hinton agar for *S. aureus* and *E. Coli*, and Mueller-Hinton agar with 5% sheep blood for *S. pneumoniae*. The solutions of the test substances: amoxicillin, amoxicilloic acid, amoxilloic acid and amoxicillin piperazyn-2,5-dion in concentrations of 0,5 µg/µl were applied in quantities of 20 µl onto paper discs with a diameter of about 6 mm. Prepared discs were applied on bacterial media and incubated for 18 hours at 35°C. After incubation, inhibition zones were measured and compared. The test was carried out in a six-fold repetition.

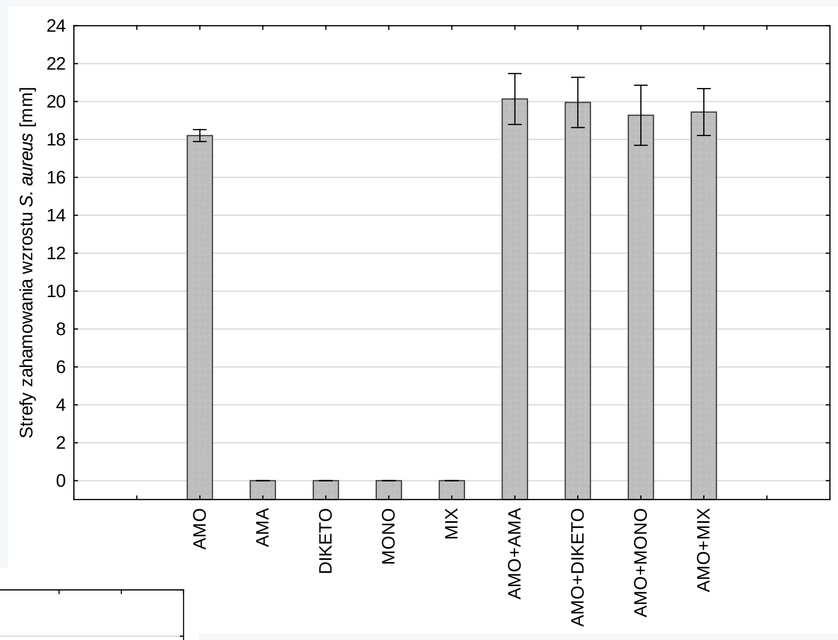
Results



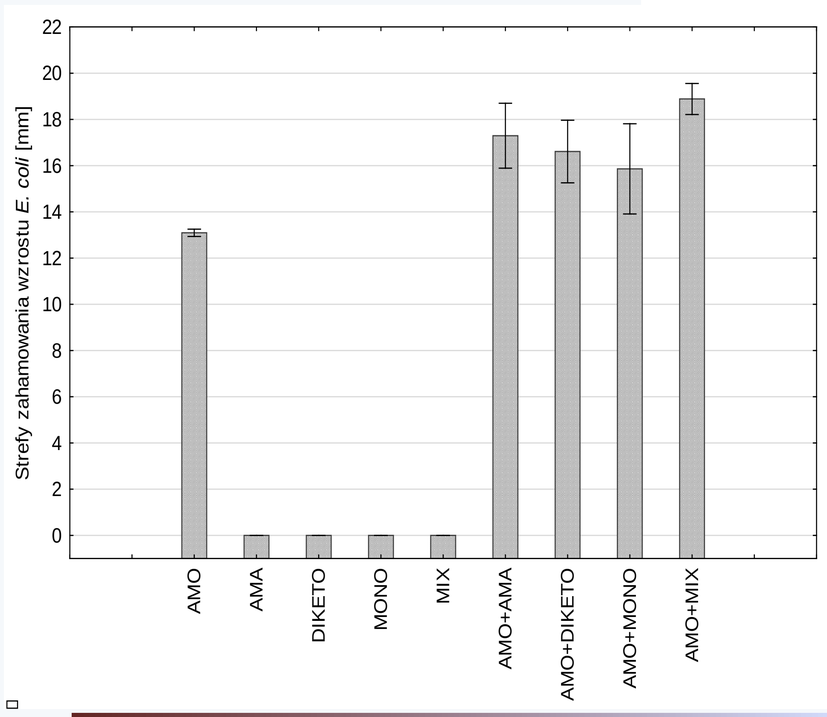
Pic.2. Areas of growth inhibition of: *Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae.*



Pic.3. Chart imaging the growth inhibition zones volume of *Streptococcus pneumoniae*. AMO – amoxicillin, AMA – amoxicilloic acid, DIKETO – amoxicillin piperazin-2,5-dion, MONO –amoxilloic acid, MIX – mixture of three metabolites in equal amounts.



Pic.4. Chart imaging the growth inhibition zones volume of *Staphylococcus aureus.* AMO – amoxicillin, AMA – amoxicilloic acid, DIKETO – amoxicillin piperazin-2,5-dion, MONO –amoxilloic acid, MIX – mixture of three metabolites in equal amounts.



Pic.5. Chart imaging the growth inhibition zones volume of *Escherichia coli.* AMO – amoxicillin, AMA – amoxicilloic acid, DIKETO – amoxicillin piperazin-2,5-dion, MONO –amoxilloic acid, MIX – mixture of three metabolites in equal amounts.

Results and conclusion

In the case of discs containing the amoxicillin alone, growth inhibition zones were 18.21 mm; 13.09 mm and 31.63 mm for *S. aureus, E. coli and S. pneumoniae*, respectively. Around the discs containing only metabolites, in concentrations equal to the concentration of amoxicillin, no inhibition zones were observed. In contrast, growth inhibition zones around the discs soaked with both, amoxicillin and its metabolites, in the 1:1 ratio were clearly larger than those obtained for amoxicillin alone. The obtained MIC values of amoxicillin indicate the possibility of inducing resistance of tested strains to amoxicillin under the influence of amoxicillin metabolites.

It is concluded that although the investigated metabolites at low concentrations do not show their own antimicrobial activity, they may increase the activity of the parent compound.