

# Antimicrobial and biocompatibility study of sorbate derivates

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## Introduction

The antimicrobial protection of orally applied, liquid dosage forms is necessary, in order to avoid contamination. Nowadays, the most commonly used groups of pharmaceutical preservatives are parabens, benzoates and sorbates. Several studies indicate, that the safety of preservatives should be reconsidered. The carcinogenic activity of parabens (Roszak et al., 2017.) and their respective endocrine effects (Nishihama et al., 2016.) and the allergenic activity of benzoates (Puri et al., 2017.) are restricting parameters of these groups. Consequently, sorbates can be considered as the safest preservatives, nowadays. In the last decades, the number of new compounds used as antimicrobial preservative, was very low and limited only to ophthalmic use. We aimed to synthesize new, sorbate derivates to improve their antimicrobial activity while retaining their advantageous biocompatibility properties. Based on previous literature results (Narasimhan et al., 2007.) we synthesized some sorbate esters and compared them to commercially available sorbic acid and potassium sorbate.

## Materials and methods

Cytotoxicity profiles of sorbic acid and its different derivatives (Ethyl sorbate and isopropyl sorbate, esters with simple alkyl chains) were assessed by cell viability assays of Caco-2 immortalized human colorectal adenocarcinoma cells with MTT and Neutral Red methods and cytometric analysis of Annexin V/propidium iodide stained cells. In vivo toxicity was tested by injecting the different chemicals into *Galleria mellonella* larvae. Antimicrobial efficacy was studied with time-kill experiments on *C. albicans*, *E. coli* and *S. aureus* reference strains.

## Results and discussion

As it can be seen on Figure 1., according to our results (Nemes et al., 2020), isopropyl sorbate is drastically more potent against *C. albicans* and *E. coli* than its parent molecule or even the ethyl sorbate. This derivative had actual killing activity at lower concentrations, whereas the compared molecules only had inhibitory effect at the same concentrations.

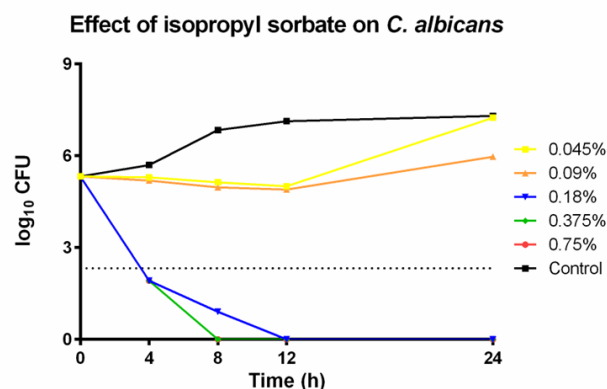


Figure 1. Antifungal effect of isopropyl sorbate

While the antimicrobial effect is many times higher, the in vitro and in vivo toxicity tests show only moderate decrease in cellular viability and larvae survivability when compared to other sorbate derivatives. However, it must be noted, that the ethyl sorbate which is structurally close to the isopropyl sorbate had similar results compared to sorbic acid and potassium sorbate which raises the question of the actual structure-activity relationship.

## Conclusion

Given these promising results, the further synthesis and investigation of other alkyl sorbate ester are carried out at our Department in order to highlight the structural relationship between antimicrobial effect and biocompatibility.

## References

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