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HYDROXYLATED FLAVONES FOR THE TREATMENT OF FUNGAL INFECTIONS

Fungal infections (FIs) are increasingly becoming a global health burden with devastating socioeconomic consequences. Although a number of pharmacological options for antifungal treatment do exist, they are currently limited to four distinct chemical classes: azoles, echinocandins, polyenes and pyrimidine analogs. The incidence of invasive FIs, accentuated by antifungal resistance strongly highlights the urgent need for the development and investigation of new antimycotics, particularly against *Candida spp.*, which represent the clinically most relevant group of pathogenic fungi. The University of Graz offers unique lead compounds of a novel class (flavonoids) that are feasible as both stand-alone agents and potentiators of currently employed antimycotics against candidiasis (FIs due to *Candida spp.*).

KEYWORDS:
FUNGAL INFECTIONS
FLAVONOIDS
ANTIMYCOTICS
POTENTIATORS
ANTI-PROLIFERATION
ANTI-BIOFILM
CANDIDA
CANDIDA AURIS

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DEVELOPMENT STATUS:
PRE-CLINICAL COMPOUNDS

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BACKGROUND

Invasive candidiasis is lethal in 30-40% of the cases, leading to at least 0.35 million deaths worldwide every year. While *C. albicans* accounts for most infections, non-albicans *Candida* show high virulence and reduced intrinsic susceptibilities to many antimycotics. Also, *Candida spp.* are among the most common causes for hospital-acquired infections in the US and Europe.

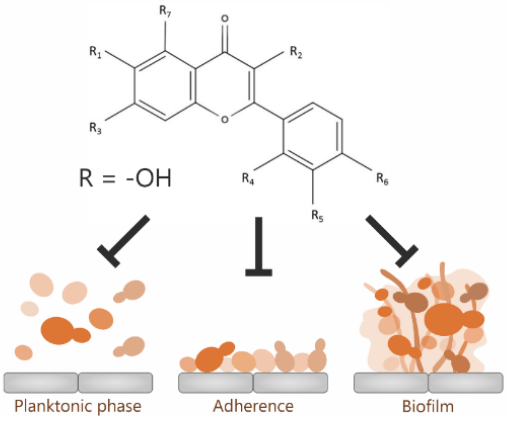

Fig.1 Pan-Candida effects of identified compounds

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The technology describes the identification of a number of hydroxylated flavonoids that demonstrate *in vitro* and *in vivo* activity against planktonic cells (the single-celled form of a fungal pathogen), thus inhibiting proliferation of the pathogen, as well as against biofilms (Fig. 1). These compounds act against both albicans and non-albicans *Candida* species and are effective either as stand-alone agents or as potentiators of known antimycotics that boost their effect. Of note, this potentiating effect is true for different chemical classes (at least azoles, echinocandins and polyenes). Altogether, these polypharmacological effects underline the potential of these compounds for treatment of severe (and lethal) candidiasis.

ADVANTAGES

- Polypharmacological effect: the same molecules act as stand-alone agents and as potentiators of different chemical classes of antifungals.
- Pan-Candida applicability: the substances act against *Candida albicans, Candida glabrata* as well as *against Candida auris.*
- Proven activity against clinical isolates (including resistant isolates).
- The chemical structure allows the implementation of medicinal chemistry to improve the lead compounds (e.g. increase half-life, pharmacological effects).
- Natural compounds: flavonoids are often human-tolerable and show no or minor side effects.

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