

The Significance of CD4 to the Number of Grown *Candida* Colonies in Oral Candidiasis Patients with HIV / AIDS

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Discussion

Basic data of this study showing isolates mostly taken from male than female (77.5% and 22.5%). The most age group is productive age groups in the age range of 26-35 years with 20 subjects (50%). In 2017 report of the Directorate General of Disease Control and Environmental Health, Ministry of Health Republic of Indonesia, found HIV/AIDS patients more male than women, and related more common in young adult which makes it more likely to engage in unsafe sexual behavior that is at risk of HIV transmission⁽⁸⁾. The domicile of HIV / AIDS patients with OC mostly came from Surabaya (90%). This is because most patients have to seek help from the nearest health center with most patients from within the city. The isolates most were taken from HIV / AIDS patients with OC who had an absolute CD4 count <100 cells / L for 28 patients (70%). This data is supported by a 2015 Indian study by Kumar that showed 71.4% of patients with a CD4 cell count <200 cells / μ L obtained by the fungus growth of *Candida* species from OC lesions⁽⁹⁾.

The evaluation of the antifungal activity of EGCG against all strains of *Candida* isolates, showed MIC values ranging from 50%-100% and MIC values fluconazole were varying. MFC produced by EGCG for

Candida sp. through the Mann Whitney test is 50%, in which concentration is able to kill the *Candida albicans* and *Candida non-albicans*. The value of fluconazole MFC was 100%, which was higher than EGCG. Previous study also found that EGCG perform better antifungal activity based on its MIC and MFC in compare to azole drugs (ketoconazole and fluconazole). EGCG showed a significant inhibitory effect in the growth of *Candida* sp especially through its ability to destroy the *Candida* biofilm and inhibit mature biofilm maintenance on its MIC. In an in vitro studies, it was shown that EGCG, EGC and ECG caused metabolic instability of *C. albicans* cultures even at the physiological polyphenol concentrations found in green tea. Of the three catechins, EGCG was found to be the strongest in slowing down the formation and maintenance of *Candida* biofilms and interfering with the formation of biofilms. EGCG was also found to be able to bind strongly with ergosterol. This activity might result in pores creation on fungal cell membranes which eventually leading to fungal cells death. It was also shown that higher EGCG concentrations inhibited the chymotrypsin-like activity of *C. albicans* in vivo which suggests that the impaired proteasol activity contributes to the metabolic and cellular structural disorders of this fungus^(10,11).

Another study with murine model of oral candidiasis showed that EGCG increased the neutrophil count and decreased the amount of infected cells by *C. albicans*. The increasing concentration of EGCG leads to the the increase of neutrophil count. This might be due to immunomodulatory effect performed by EGCG itself which also beneficial for oral candidiasis therapy, especially in immunocompromised patient as in HIV/AIDS patient⁽¹²⁾.

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EGCG also produced synergistic effect when used together with fluconazole or ketoconazole resulting in higher fungicidal activity. The results in 4 species with EGCG (MFC) alone resulted in a reduction of 95.13%, while in synergistic combination resulted in a decrease of 92.27% for fluconazole and 97.51% for ketoconazole, compared to controls. The MIC value of fluconazole/EGCG or ketoconazole/EGCG decreased 3 to 4-fold in compare to the inhibitory effect of those drugs alone. Another study also found that the mechanisms of EGCG inhibitory effect on *C. albicans* is obtained via key enzymes in the biosynthesis of purines, pyrimidines and some amino acids, and independent of pH^(10, 11).

Conclusions

These results highlight the potential of EGCG as an antifungal drug candidate. Based on the data showed antifungal activity with fungistatic and fungicidal effect better than fluconazole. We acknowledge the need to determinate the active compounds that inhibit germ tube formation and their mechanisms of action. However, if these substance is planned to be used in medicinal purposes, issues of safety and toxicity will need to be addressed in the next research.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

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