Vulvovaginal candidiasis (VVC) caused by Candida albicans is a common infection that has been considered an important public health problem. The most important C. albicans virulence factor is the ability to form biofilms, which in the vaginal environment may be formed on epithelium and on intrauterine devices promoting VVC. Despite it has been shown that VVC has a hormonal dependency the effects of progesterone on biofilm formation by C. albicans are still poorly understood. Thus, this work aimed to deepen the knowledge in that field by studying how the presence of progesterone modulates the transcriptional response of C. albicans biofilms, a knowledge that is essential to identify possible targets to control VVC. The progesterone effects on C. albicans biofilms were evaluated in terms of total biomass, metabolic activity, structure and matrix composition, while the transcriptional response was assessed by using species-specific microarrays. The results obtained showed that progesterone was able to reduce C. albicans biofilm, decreasing its biomass, structural cohesion, matrix production and matrix carbohydrate content. Additionally, progesterone decreased the expression of several genes involved in the carbohydrate metabolism and biological adhesion including four genes known to be required for C. albicans ability to form biofilms (TEC1, PBR1, AHR1 and CR_01410C_A). Considering that the vaginal tract is one of the main driveways for the development of C. albicans infections, the identification of genes that may determine the ability of this yeast to survive and form biofilm in the vaginal environment may contribute to the disclosure of new targets to treat/prevent VVC.