S. epidermidis is one of the most common causes of medical device-related infections, being associated with increased patients’ morbidity but also with massive additional financial burden. Hence, several efforts have been made to identify S. epidermidis virulence determinants, including the mechanisms behind biofilm formation and antibiotics tolerance. However, the great majority of these studies were performed using artificial media, which composition does not reflect in vivo conditions, and in the absence of host factors reducing the clinical relevance of those findings. Thus, the aim of this work was to evaluate the influence of host factors present in human plasma on S. epidermidis growth rate, biofilm formation capacity and tolerance to antibiotics. The presence of human plasma (5 to 20%) in the culture medium (Tryptic Soy Broth) significantly decreased both growth rate and biofilm formation ability. The greater the plasma concentration (20%), the greater the inhibitory effect observed (2 log_{10} reduction in growth and 3-fold less biofilm biomass). Interestingly, different results were obtained when the brand of the medium was changed. Thus, due to the inherent variability of complex media, chemically defined medium (CDM) was used instead. Respecting the bacterium growth rate, once more, the greater the plasma concentration, the greater the inhibition observed although with CDM the impact was less pronounced (1 log_{10} reduction in the presence of 20% of plasma). However, different from what was observed with TSB, no differences were found on biofilm formation capacity. In addition, our data showed that human plasma decreased the effect of vancomycin as 1.3 log_{10} reduction was observed in the absence of plasma and only 0.5 in the presence of 20% of plasma. Overall, our results highlight the importance of introducing host factors in in vitro assays in order to better mimic in vivo conditions consequently increasing the clinical significance of the results obtained.