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Anti-herpesviral effects of a novel broad range anti-microbial quaternary ammonium silane, K21

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ABSTRACT

We have created a novel quaternary ammonium silane, K21 through sol-gel chemistry, using an ethoxylated version of an organosilane quaternary ammonium compound and TetraEthyl Ortho Silicate (TEOS) as precursors. Previous studies using the precursor molecule quaternary ammonium compounds (QACs) and a methacryloxy version of K21, primarily designed for use in dental healthcare, have shown inhibited growth properties against several types of gram-positive and gram-negative bacteria including *Escherichia coli*, *Streptococcus mutans, Actinomyces naeslundii and Candida albicans etc*. Here we tested the effect of K21 on HSV-1, HHV-6A and HHV-7 in *in vitro* cell culture infection models. Our results show growth inhibitory effect of K21 on HSV-1, HHV-6A and HHV-7 infection.

1. Introduction

Quaternary ammonium compounds (QACs) have both surfactant properties and broad-spectrum antimicrobial activity and hence are widely used as anti-bacterial agents (McBain et al., 2004). Although the exact mechanism behind the antimicrobial properties of QACs is not fully understood, it is well accepted that QACs can solubilize phospholipid bilayers (Salton, 1968) leading to progressive cell lysis. Previously we have created a methacryloxy version of QAC, which was proven to be effective against the growth of varieties of pathogenic organisms including *Escherichia coli*, *Streptococcus mutans, Actinomyces naeslundii, Porphyromonas gingivalis and Candida albicans* (Gong et al., 2012a, 2014, 2012b). Recently, contact-killing antimicrobial activities of this compound were elucidated in a double-blind randomized clinical trial (Liu et al., 2016). In order to design a QAC with enhanced antimicrobial properties, we developed ethoxylated version of the QAC, called K21, which was tested effective against *Porphyromonas gingivalis* and *Enterococcus faecalis* (Meghil et al., 2015). With an intention of using K21 in dental materials, we tested efficacy of K21 against some of the human herpes viruses including HSV-1, HHV-6A, HHV-6B and HHV-7 that reside in the human oral cavities and are shed in the saliva to induce infection.

Here, we report antiviral nature of a novel compound K21, which acts as a prophylactic agent and reduces the infectivity of HSV-1, HHV-6A and HHV-7 at non-toxic concentrations. Our studies indicate reduced *in vitro* viral load in presence of K21 demonstrated at both DNA and protein levels.

2. Material and methods

2.1. Drug

The compound K21 was obtained from KHG fiteBac technologies, USA.

2.2. Cell lines and viruses

Primary human foreskin fibroblasts (HFFs) (ATCC SCRC-1041)

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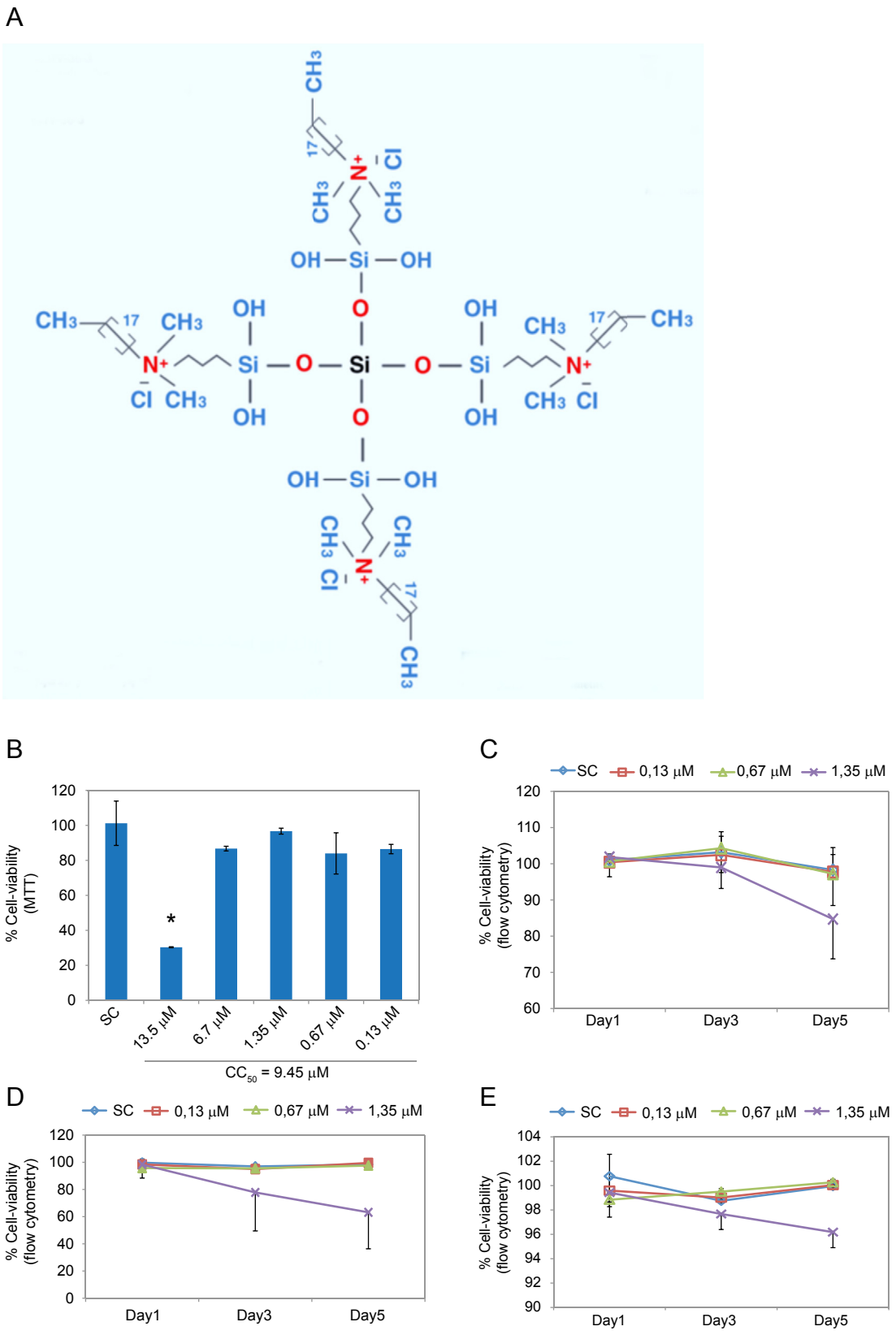

Fig. 1. Structure and cytotoxicity of K21. (**A**) Molecular structure of K21 molecule. (**B**) Cell viability (MTT) assay in primary human foreskin fibroblasts (HFFs) to determine cytotoxic dose (CC_{50}) of K21. HFFs were seeded into 96-well plates (10^3 cells/well). At 24 h in culture with varying amounts of K21, cells were analyzed for viability by MTT assay. Results show the mean % cell viability relative to solvent control treated cells (SC) from two repeated experiments performed in triplicate. $^*p < 0.05$. CC_{50} value was calculated to be 9.45 µM from the calculated slope equation. (**C**) Effect of K21 up on prolonged exposure to HFFs was studied by growing the cells in the presence or absence of different concentrations of K21 from 1 to 5 days and subsequently staining the cells with Annexin V and PI. Cells were counted and analyzed using flow cytometry. Data represents ±SEM of three independent experiments carried out on 3 different days. Similar cytotoxicity experiments were carried out in HSB-2 (**D**) and SupT-1 (**E**) cells.