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Medical Implications of Antimicrobial Coating Polymers- Organosilicon Quaternary Ammonium Chloride

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Abstract

Hospital-Associated Infections (HAI) are commonly caused by the invasive device and prosthesis implanted in the body. The practice of coating antimicrobial agents on biomedical surfaces or modifying the composite resin with such agents has been shown effective in reducing the incidence of HAI. Quaternary Ammonium Chloride (QAC) salts and the Organosilicon derivatives (OrganoSiQAC) are surface active to serve these applications. Clinically, Benzalkonium chloride (BAC) is effective against a board range of microorganisms. However, it has been recognized as the source of several hospital outbreaks due to contamination with gram-negative bacteria. Safety aspects such as potential toxicities and in vivo efficacies were poorly defined. On the other hand, physical antimicrobial polymers formed by OrganoSiQAC compounds were found to be chemically stable and nonleachable from the bonded surface, whereas the biocidal effects were exerted by the end satellite QAC groups. Recent studies have also reported the application of such bioactive films on animated surfaces such as skin and mucosal lining. This opens the future perspective with multiple applications in infection control, in the regards of reduce use of antibiotics, treatment alternatives for multiple antibiotic resistance, blocking the route of transmission of specific organisms in clinical and community settings.

Keywords: Ammonium chloride; OrganoSiQAC compounds; Antibiotic resistance

Introduction

Quaternary ammonium compounds (Quats) especially, the chloride salts are extensively used for clinical purposes such as preoperative disinfection of unbroken skin, application to mucous membranes, and disinfection of noncritical surfaces [1]. The cationic properties of Quats contribute to a variety of applications as disinfectants, antiseptics, herbicides, spermicides, detergents, and sanitizing agents [2]. Organosilicon Quaternary Ammonium Chloride (OrganoSiQAC) salts are cationic polymeric materials that typically contain a Quaternary Ammonium Chloride (QAC) end group in the organosilicon architecture. Such organosilicon-substituted amines are well known active surfactant-mediated agents that are able to cause polymerization immediately after contacting any surface. Organosilicon chemistry is the designated field of science studying the properties and reactivity of all organic compounds containing carbon-silicon (Si-C) bonds. In this mini-review, the authors are particularly interested in exploring two relative Quats – QAC and Organiosilicon; briefly discuss their chemistry and synthesis, utilization in healthcare as antimicrobial agents, safety issues, major shortcomings and future perspective.

The Chemistry of Quats and OrganoSiQAC

Quats share a common tetra alkyl ammonium structure of $N^{+}4xR$ where a nitrogen (N^{+}) atom is directly linked to four alkyl groups (R), forming positively charged polyatomic ions with a variety of complexity [3]. In the process of quaternization, a tertiary amine can be converted to Quats by alkylation, and typically one of the alkyl groups is larger than the others [4]. Benzalkonium Chloride (BAC), the most widely used QAC-based antiseptic in healthcare, is synthesized from the long-chain alkyldimethylamine and benzyl chloride:

$$CH_3(CH_2)_nN(CH_3)_2 + ClCH_2C_6H_5 \rightarrow [CH_3(CH_2)_nN(CH_3)_2CH_2C_6H_5]^{+}Cl^{-}$$

Besides BAC, other antimicrobial QAC compounds, such as alkyldimethylbenzylammonium chloride and didecyldimethylammonium chloride, are also used as active antimicrobial agents.

Silicon (Si), on the other hand is tetravalent and tetrahedral that allows the formation of organosilicon amines with basic structure of Si·4xR, whereas OrganoSiQAC contains typically a QAC substitute as one of the alkyl groups [5]. When compared with the carbon-carbon (C-C) bonds of hydrocarbons, Si-C bonds are more readily to be broken because of the weaker bond dissociation energy (Si 451 kJ/mol vs C 607 kJ/mol). The greater electronegativity (C 2.55 vs Si 1.90) of carbon atom contributes also to the polarization of Si towards the carbon. Compare with Quats and QAC which are entirely hydrocarbon in nature, the cationic OrganoSiQAC molecules have lower micelle concentrations and provide lower surface tension due to the presence of silicon in their hydrophobic groups. Despite organosilicons are highly hydrophobic, quaternization could further increase the water solubility of the compound. The synthesis of OrganoSiQAC involves multiple steps based on either one of the two catalytic methods: (1) the formation of tertiary amino silicon by Si-H addition reaction, followed by reaction with haloalkane; and (2) the Menschutkin reaction between halogenoalkyl silicone unit and tertiary amines. Recently, Li et al. [6] has described a one-step Menschutkin reaction without catalyst and successfully synthesized two OrganoSiQAC molecules, namely Diethyl-benzyl-[3-methyldimethoxyl]silpropyl ammonium chloride (DEBSAC) and Trimethyl-[3-methyldimethoxyl]silpropyl ammonium chloride (TMSAC) as shown in Table 1. Both products were surface active and antibacterial against *Escherichia coli* (*E. coli*) (Table 1).

Utilization of QAC as Antimicrobial Surfactant

Hospital-Associated Infections (HAI) are commonly caused by the invasive device and prosthesis implanted in the body. The practice of coating antimicrobial agents on biomedical surfaces or modifying the composite resin with such agents has been shown effective in reducing

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the incidence of HAI. This is attributed by the surfactant property of QAC and OrganoSiQAC compounds, which allows the absorption of the compound molecules to form a protective coating and the reaction with the surfaces to form a new antimicrobial film, respectively. The underlying anti-infective mechanism of such surfactant activity lies on the prevention of microorganism adherence to resist biofilm formation [7,8]. 'Powder test' has confirmed the theory of absorption of cations to prepare antimicrobial surfaces, especially on fibers and textiles [2]. Cations alone were discovered to be responsible for antimicrobial behavior [2].

Studies have demonstrated that colonization of a range of pathogenic organisms, including gram- positive and negative species as well as *Candida albicans* were inhibited by coating the surface of central venous catheters with BAC [9,10]. BAC-modified orthodontic composite resin has shown to exert inhibitory activity against *Streptococcus mutants* (common cause of dental caries), without affecting the bond strengths of the material [11]. However, such antimicrobial properties on surfaces were merely evidenced by in vitro experiments [9-12]. The in vivo effectiveness is doubtful, since in the study of Imbert et al. [10], the inhibition of *C. albicans* adherence exerted by BAC has become ineffective when the plastic surface was layered with an extracellular matrix gel [10]. Nonetheless, numerous QAC-based surfactants are nowadays developed into nonascale that could also serve as vesicles for drugs. A successful case was reported by Matl et al. [12] that hydrophilic antibiotic drugs were bond together with QAC compounds onto the lipophilic surfaces of Polytetrafluoroethylene (PTFE) prostheses, where antibiotics were being delivered in vivo after the prosthetic implantation.

Despite it is already the most studied QAC compound, since 1994, BAC has been classified by the U.S. Food and Drug Administration as a Category IIISE active antiseptic, which means data is insufficient to classify as safe and effective [13]. Epidemiologically, several hospital infection outbreaks were associated with contamination of BAC solutions with bacteria, especially the gram negative species [14]. Several organisms, mainly the glucose non-fermentative bacillus including *Pseudomonas aeruginosa* (an important causative agent of nosocomial infections), were viable to grow in the diluted BAC solution and 0.02% BAC-soaked cotton balls [15]. More specifically, BAC solutions contaminated with *Serratia marcescens* have been associated with reported cases of lethal infections such as meningitis [16] and septic arthritis [17]. Nakashima et al. [18] have reported the survival ability of *Serratia marcescens* in BAC solutions. Apart from the contamination issues, the biocidal nature of QAC compounds has also drawn the concerns about resistance development [19] and potential toxicities [20]. Several bacterial isolates, including *Staphylococcus aureus*, displaying decreased susceptibility to QACs have been reported [21]. Particularly, QAC compounds of lower molecular weight are gradually released from the bound surface, leading to the loss of antimicrobial activity over time while such leaching particles could also be toxic in vivo if it is not properly controlled [20].

The Era of OrganoSiQAC and Future Perspective

In general, since there is a new physical layer formed on the surface, polymeric biocides are known to have certain advantages: (1) stable and without releasing low molecular weight toxic products to the environment; (2) no problem of residual toxicity; (3) durable and sustainable antimicrobial activity; and (4) common bacterial strains do not appear to develop resistance [22]. Thermal stable polysiloxane polymers containing N,N'-dialkylimidazolium halide groups are very potent against a broad spectrum of bacteria [22,23]. A research team led by Walters et al. [24] has first demonstrated the formation of a waterproof firm with an OrganoSiQAC, known as Quat-Silsesquioxane (3-(trimethoxysilyl)-propyldimethyloctadecyl ammonium chloride) through hydrolysis on glass surfaces. Quat-Silsesquioxane has been tested in mammal animals and revealed its extremely low toxicities, in term of tetratogenicity and abnormal foetus development [25,26]. As shown in Figure 1, when immobilized on the reactive surface, the QAC compartment of Quat-Silsesquioxane acts as the functional group for microbicidal activities against representative species of alga [24], bacteria and fungi [23]. In late 90s, Saito and colleagues [27] developed a spray solution contains a mixture of Quat-Silsesquioxane and spherical silica particles, which improve the efficiency and quality of bioactive film, using a spray-dry procedure. A nonleachable adhesive coating was successfully polymerized on the oxidized silicone rubber surface upon silanization, and provided stable and long-lasting antimicrobial protection both in vitro and in rats *in vivo* [28]. Later on, the shortcomings of peeling off and be scraped off from the surface were addressed by the layer-by-layer self-assembly approach [29]. Multilayer coatings for medical implants supply the dual functions to prevent bacterial attachment and to provide versatility of tunable release of therapeutic agents [30]. Recently, a new nanotechnology known as JUC (Brand name) was shown to be beneficial in preventing the growth of *E. coli* (a common cause of Urinary Tract Infection (UTI)) on the surface

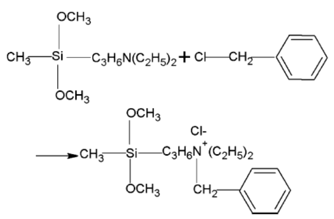
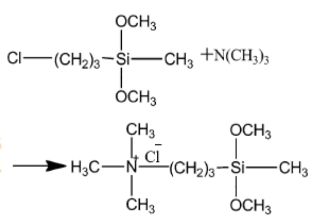
Compound	Reaction	Raw materials used	Reaction condition
DEBSAC		(1) N,N-diethyl-aminopropyl-methyldimethozysilanes (2) Benzyl chloride Molar ratio = 1:1.2	Reflux at 80°C for 22 hours.
TMSAC		(1) trimethylammonium ethanol solution (30%) (2) γ-chloropropylmethyl-dimethoxysilane Molar ratio = 1.3:1	Stir the mixture at 90°C for 12 hours.

Table 1: The one-step non-catalytic synthesis of two OrganoSiQAC compounds [6].

of siliconized latex urinary catheters; and this property was reported to reduce the incidence rate of catheter-associated UTI, from 13.04% to 4.52%, in a randomized controlled clinical trial with 1,150 patients [31]. So far, the antimicrobial coatings discussed were all applied on inanimate surfaces, but could they be used on animate surfaces such as hands and skin? (Figure 1).

The JUC spray is marketed as a physical antimicrobial dressing for wound care, its formulation composed of 2% OrganoSiQAC as key ingredient, despite the exact OrganoSiQAC formulae has not been disclosed by the manufacturer. This forms a cutting-edge technology indicative to be applicable on skin and mucosal surfaces. The idea is simple enough underlying the principle that avoidance of microbial adherence on the surface and surrounding of wounds would prevent wound infection, and thus favor wound healing. At first, it was believed that microcidal effects of polymers formed by OrganoSiQAC compounds were proportionally correlated with the length of the carbon chain in the alkyl moieties and their abilities of polymerization [32]. Actually, the killing activities are dependent on the satellite end groups determined by the formation of unimolecular micelles as consequence of the polyoxazolines aggregation behavior, instead of the polymeric chain lengths [33]. Take JUC as example, immediately after contacting any surfaces, an invisible antimicrobial layer with dual overlaying structure: the bonded film and the positive charge film are produced. The bonded film aims to secure the adhesion to the surface, whereas positive charge film contains polycations bearing considerable positive charge may destructively interact through electrostatic forces with the negatively charged bacteria walls and membranes leading to the killing effects (Figure 2) [22,34].

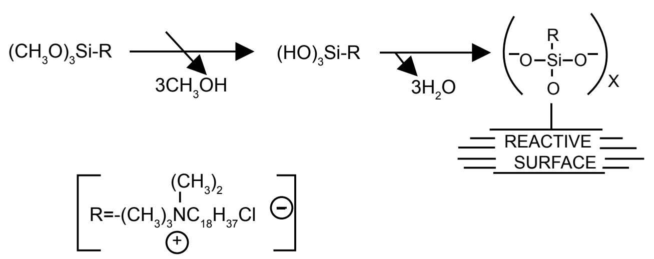


Figure 1: Diagram adopted from [23,24] displaying the hydrolysis reaction of Quat-Silsesquioxane on glass surface. Microcidal activity is exerted by the R group exposed at the bound surface.

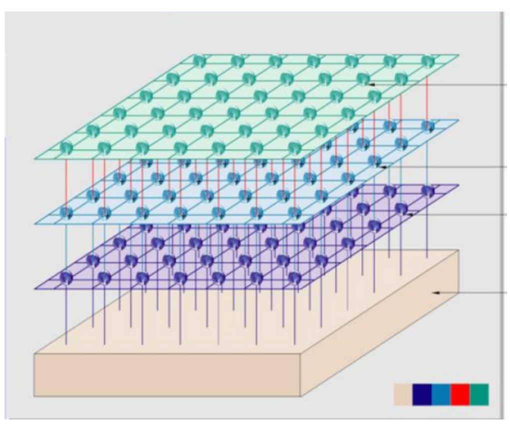


Figure 2: Diagram adopted from [34] showing the dual layers form by JUC spray to exhibit antimicrobial function.

Clinically, several studies conducted in Mainland China have already been demonstrated the effectiveness of JUC spray on preventing post-operative infection and reducing wound healing time in patients who received different surgical procedures, such as circumcision in males [35] and tumor removal of oral cancer patients [34]. In neck and head cancer patients who are receiving radiation therapy, JUC when applied at the onset of acute dermatitis, was shown to relieve the itching and pain sensation, promote wound healing, and reduce the incidence of secondary infection by 13% [36]. In another study conducted with patients in Intensive Care Unit (ICU) of a major Hong Kong hospital, the incidence rate of ventilator-associated pneumonia was significantly reduced from 54.2% to 8.4% after the application of JUC to the oral and nasal cavity [37]. Furthermore, a case of scalp abscess infected with methicillin-resistant *Staphylococcus aureus* (MRSA) was successfully treated solely with JUC spray without other form of treatment including antibiotics [38]. This reported case supported not only future investigation regarding the therapeutic roles of JUC and other OrganoSiQAC, but also suggested novel treatment alternative for multiple drugs resistance the potential reduction of antibiotics usage. In our laboratory, the efficacy of using JUC as a long-lasting hygienic handrub product was evaluated according to the requirements of European Standard, and another study was underway to investigate the effect of JUC in blocking MRSA transmission in a hospital ward environment. The OrganoSiQAC-based antimicrobial nanotechnology could be the trend of 'modern tools' to address important issues of infection control: reduce use of antibiotics, treatment alternatives for multiple antibiotics resistance, blocking the route of transmission of specific organisms in clinical and community settings.

Conclusion

In summary, the chemistry of QAC and OrganoSiQAC compounds has formed the fundamental concept about physical antimicrobial surface. The current body of literature identifies BAC and Quat-Silsesquioxane as typical clinically used. Newly emerging OrganoSiQAC nanotechnology such as JUC may be the future direction of research and application.

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抗菌涂层聚合物的医学意义 - 有机硅季铵盐类化合物

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摘要

院内感染（HAI）常由侵入性器械和假体植入引起。在生物医学表面上涂上抗菌剂或用抗菌剂让复合树脂改性的做法已被证明能有效减少院内感染的发生率。季铵盐类化合物（QAC）和有机硅衍生物（有机硅季铵盐类化合物（OrganoSiQAC））在这些应用上具有表面活性。在临床上，苯扎氯铵（BAC）能有效对抗多种微生物。然而，它已被认为是革兰氏阴性菌的污染引起的院内疾病暴发的始作俑者。安全性方面，如潜在的毒性和体内疗效都不好界定。另一方面，人们发现，有机硅季铵盐类化合物形成的物理抗菌聚合物在胶联的表面上具化学稳定性，且不可过滤，而杀灭微生物的作用由末端QAC基团施加。最近的研究还报道了这种生物活性薄膜在活体表面，如皮肤和粘膜层的应用。在感染控制上的多种应用将为未来开拓前景，从而减少抗生素的使用，取代耐药的抗生素进行治疗，在临床和社区环境阻断特定微生物的传播途径。

关键词：氯化铵、有机硅季铵盐类化合物、抗生素耐药性

引言

季铵化合物中，特别是氯化铵被广泛用于临床用途，例如未破损皮肤的术前消毒，在粘膜上的应用，非临界表面的消毒[1]。季铵化合物的阳离子属性带来了各种应用，如消毒剂、杀菌剂、除草剂、杀精子剂、清洁剂，和消毒剂[2]。有机硅季铵化合物是阳离子高分子材料，通常在有机硅结构中含有季铵化合物末端基团。这种有机硅取代的胺是公认的表面活性剂介导剂，能够在接触任何表面后立即引起聚合。有机硅化学是研究含碳-硅（SI-C）的所有有机化合物的性质和反应的特定科学领域。在本小型综述中，作者们特别感兴趣的是探索两种相关的季铵盐类化合物 - 季铵盐类化合物和有机硅：简要讨论了它们的化学性和合成，作为抗菌剂在医疗领域的应用，安全问题，主要缺点和未来前景。

季铵化合物和有机硅季铵盐类化合物的化学性

季铵化合物都有四烷基铵结构N+4xR，N+直接与四个烷基(R)相连，形成复杂的多种带正电的多原子离子[3]。在季铵化的过程中，季铵可以通过烷化被转换为季铵盐类化合物，并且通常其中一个烷基比其他烷基要大[4]。苯扎氯铵（BAC），在医疗领域应用最广泛的基于季铵盐类化合物的抗菌剂，由烷基二甲基胺和氯化甲基苯的长链合成：

$CH_3（CH_2）_nN（CH_3）_2 + ClCH_2C_6H_5 \rightarrow [CH_3（CH_2）_nN（CH_3）_2CH_2C_6H_5]^+ Cl^-$

除苯扎氯铵以外，其他抗菌季铵盐类化合物，如烷基二甲基苄基氯化铵和二癸基二甲基氯化铵，也用作活性抗菌剂。

另一方面，硅（Si）是四价和四面体，让带有Si·4xR基本结构的有机硅铵形成，而有机硅季铵盐类化合物通常含有季铵盐类化合物来替代烷基之一[5]。与碳氢化合物的碳 - 碳（C-C）键相比，硅-碳键更容易被破坏，因为较弱的键裂解能（硅 451千焦/摩尔 vs 碳 607千焦/摩尔）。碳原子更大的电负性（碳 2.55 vs 硅 1.90）也有助于碳硅键向碳原子的方向极化。与在本质上完全是碳氢化合物的季铵化合物和季铵盐类化合物相比，阳离子有机硅季铵盐类化合物的分子由于在疏水基团中存在硅，具有较低的胶束浓度，并提供较低的表面张力。尽管有机硅具有高度疏水性，季铵化可以进一步提高化合物的水溶性。有机硅季铵盐类化合物的合成涉及多个步骤，基于以下两个催化方法中的任一个：（1）通过硅-氢的加成反应、随后与卤代烷反应形成季胺硅，，（2）卤代烷基硅和季胺之间的门秀金反应。近日，李等人描述了一个无需催化剂的单步门秀金反应，[6] 并成功合成了两种有机硅季铵盐类化合物分子，即二乙基 - 苄基 -[3-甲基二甲氧基] 硅丙基氯化铵（DEBSAC）和三甲基[3-甲基二甲氧基] 硅丙基氯化铵（TMSAC），如表1中所示。这两款产品均具有表面活性，并对大肠杆菌有抗菌作用（表1）。

运用季铵盐类化合物作为抗菌表面活性剂

院内感染（HAI）常由侵入性器械和假体植入引起。在生物医学表面上涂上抗菌剂或用抗菌剂让复合树脂改性的做法已被证明能有效减少院内感染的发生率。这是由于季铵盐类化合物和有机硅季铵盐类化合物具有表面活性剂性质，可吸收复合分子形成保护膜，分别与表面发生反应形成新的抗菌膜。这类表面活性剂作用的根本抗感染机制在于防止微生物粘附，从而阻止生物膜的形成[7,8]。"粉末试验"已确认了吸收阳离子来制备抗菌表面的理论，特别是在纤维和纺织品表面的抗菌作用[2]。研究发现仅阳离子具有抗菌作用[2]。

研究表明，使用苯扎氯铵涂覆中心静脉导管表面可抑制革兰氏阳性和阴性菌，以及白色念珠菌等很多病原微生物的定植[9,10]。研究表明，苯扎氯铵改性正畸复合树脂可抑制变形链球菌（龋齿常见的原因），而不影响材料的粘结强度[11]。但在这些表面上的抗菌性能只能通过体外实验证明[9-12]。体内有效性仍不确定，因为在 Imbert 等人[10]的研究中，使用细胞外基质凝胶压植塑料表面时，苯扎氯铵抑制白色念珠菌粘附性的作用就变得无效[10]。尽管如此，许多季铵盐表面活性剂如今已发展成为纳米级，也可作为药用囊泡。Matl 等人报道了一个成功的案例[12]，假体植入术后抗生素进入体内，亲水性抗生素药物与季铵盐类化合物一起粘结到聚四氟乙烯（PTFE）假体的亲脂性表面上。

尽管自 1994 年以来，苯扎氯铵已经是研究最多的季铵盐类化合物，但美国食品药品监督管理局已将其列入 IIISE 类活性杀菌剂，这意味着数据不足以证明其安全有效[13]。从流行病学角度来看，几次医院感染暴发与苯扎氯铵溶液的细菌污染有关，尤其是革兰氏阴性菌[14]。有几种微生物，主要是包括绿脓杆菌（院内感染的重要病原体）在内的葡萄糖非发酵菌，可在稀释的苯扎氯铵溶液及 0.02% 苯扎氯铵浸渍的棉球中生长[15]。更具体地说，有粘质沙雷氏菌污染的苯扎氯铵溶液与报告的脑膜炎[16]和化脓性关节炎[17]等致死性感染有关。Nakashima 等人[18]报告了苯扎氯铵溶液中粘质沙雷氏菌的存活能力。除了污染问题之外，季铵盐类化合物的杀生物性也引起了耐药性[19]和潜在毒性[20]问题。研究报告表明，金黄色葡萄球菌等几种细菌菌株对季铵盐的药敏性有所降低[21]。特别是，低分子量的季铵盐化合物逐渐从结合表面释放出来，导致其抗菌活性随着时间而丧失，如果没有适当控制，那么浸析颗粒在体内可能还具有毒性[20]。

有机硅季铵盐类化合物的时代及未来展望

总体来说，由于在表面形成新的物理层，所以聚合杀菌剂有一定的优势：(1) 稳定，不会将低分子量有毒产品释放到环境中；(2) 没有残留毒性问题；(3) 抗菌活性持久且具有可持续性；(4) 常见的细菌菌株不会产生耐药性[22]。含 N， N' -二烷基咪唑卤化物基

团的热稳定聚硅氧烷聚合物对杀灭广谱细菌是非常有效的[22,23]。以 Walters 等人为首[24]的一个研究小组首次使用一种被称为四聚倍半硅氧烷（[3-(三甲氧基硅基)丙基]氯化铵）的有机硅季铵盐类化合物，通过玻璃表面的水解，证明了防水薄膜的形成。四聚倍半硅氧烷已在哺乳类动物中进行了试验，并表明其在致畸性以及胎儿发育异常方面的毒性极低[25,26]。如图 1 所示，固定在反应表面时，四聚倍半硅氧烷的季铵盐作为杀灭藻类[24]、细菌和真菌[23]代表性菌种的杀菌活性官能团。在 90 年代后期，Saito 及其同事们[27]开发了一种含有四聚倍半硅氧烷和球形二氧化硅颗粒的喷雾溶液，该溶液使用喷雾干燥过程的混合物可以提高生物活性薄膜的效率和质量。不可浸出的粘性涂层烷化后被成功地聚合在氧化硅橡胶表面，在体外和大鼠体内具有稳定性和持久的抗菌保护[28]。后来，表面剥落和刮掉的缺点通过层层自我组装的方法得以解决[29]。医疗植入物的多层涂层具有双重职能，防止细菌附着，并可调节治疗药物的释放[30]。最近，一种被称为 JUC（品牌名称）的新的纳米技术显示出可以有效防止硅化乳胶导尿管表面大肠杆菌（一种常见的尿路感染（UTI）原因）的生长，在一项 1150 例患者随机对照临床试验中，这个特性被报道可以减少导尿管相关性尿路感染的发病率，从 13.04％降至 4.52％[31]。到目前为止，所讨论的抗菌涂层都应用在无生命的表面上，但是他们能应用在有生命的表面，例如，手部和皮肤上吗？（图 1）

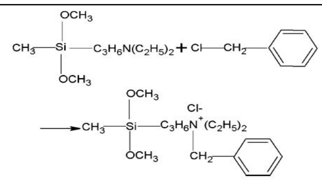
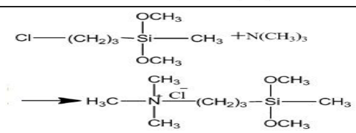
化合物	反应	使用的原材料	反应条件
DEBSAC		(1) N， N-二甲基氨丙基甲基二甲氧基硅烷、(2)氯化苯 摩尔比 = 1:1.2	在 80℃下回流 22 小时
TMSAC		(1)三甲基乙醇溶液 （30%） (2) γ -氯丙基甲基二甲氧基硅烷 摩尔比 =1.3:1	将混合物在 90℃下搅拌 12 小时。

表 1：两种有机硅季铵盐类化合物的非催化单步合成[6]。

JUC 喷雾剂在市场上作为伤口护理的物理抗菌敷料，其配方是由 2％的有机硅季铵盐类化合物作为关键成分，尽管制造商并没有披露确切的有机硅季铵盐类化合物配方。这是一种尖端技术，适用于皮肤和粘膜表面。这个理念在基本原则下显得十分简单，即避免微生物粘附在表面上和伤口周围以防伤口感染，从而有利于伤口愈合。起初，人们认为有机硅季铵盐类化合物形成的聚合物杀微生物的作用与烷基部分碳链的长度及其聚合能力成正比[32]。其实，杀菌活性是依赖于聚噁唑啉聚集后形成单分子胶束决定的末端基团，而不是在聚合物链的长度[33]。以 JUC 为例，接触任何表面后，立即形成隐形抗菌层，有双层复式结构：产生胶联膜和正电荷膜。胶联膜的目的是确保粘附表面，而正电荷膜中含有聚阳离子，带大量的正电荷，可以通过破坏性的静电力与带负电荷的细菌细胞壁和细胞膜相互作用，形成杀菌作用（图 2）[22,34]。

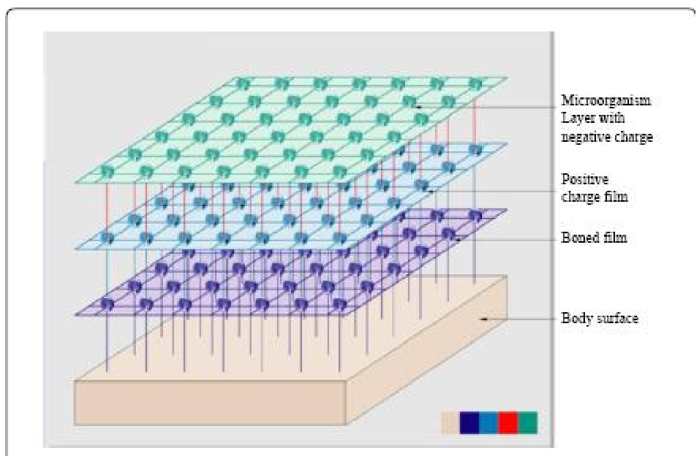


图 2：[34]中的图，显示 JUC 喷雾剂形成的复式结构，可产生抗菌作用

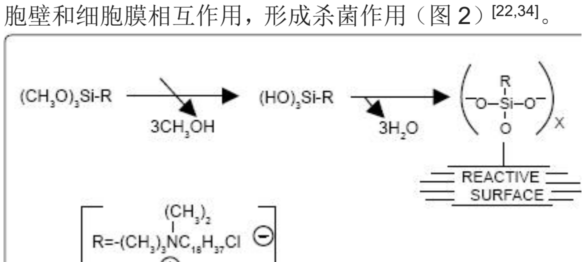


图 1：[23,24]中的图，显示四聚倍半硅氧烷在玻璃表面的水解反应。杀微生物的作用通过作用于胶联表面的 R 基团得以展示。

临床上，在中国内地进行的一些研究已经证明了 JUC 喷雾剂对于接受男性包皮环切术[35]和口腔癌瘤切除[34]等不同手术患者在防止术后感染和减少创面愈合时间方面的有效性。在接受放疗的头颈部癌瘤患者中，当用于急性皮炎时，结果表明，JUC 可以减轻瘙痒和疼痛感，促进伤口愈合，减少 13％的继发感染发生率[36]。在香港一家大型医院对重症监护室（ICU）患者进行的另一项研究中，JUC 应用口腔和鼻腔后，呼吸机相关肺炎的发病率从 54.2％明显降低到 8.4％[37]。此外，耐甲氧西林金黄色葡萄球菌（MRSA）感染的头皮脓肿病例以 JUC 喷雾剂单用

成功治疗，没有联用抗生素等其他形式的疗法[38]。该报告的病例不仅支持了 JUC 和其他有机硅季铵盐类化合物治疗作用的未来调查，而且建议了多重耐药的新型替代治疗，潜在减少了抗生素的使用。在我们的实验室中，使用 JUC 作为长效的卫生搓手液产品，根据欧洲标准的要求评估效果，并且正在进行另一项研究以探讨 JUC 阻断 MRSA 在医院病房环境中传播的作用。基于有机硅季铵盐类化合物的抗菌纳米技术可能是人们趋向使用的“现代工具”，可以解决感染控制的重要问题：减少抗生素的使用，多重耐药性的替代治疗方案，在临床和社区环境中阻断特定微生物的传播路线。

结论

总之，季铵盐类化合物和有机硅季铵盐类化合物的化学性形成了物理抗菌表面有关的基本概念。目前的文献将苯扎氯铵和四聚倍半硅氧烷作为典型的临床使用材料。JUC 等新兴有机硅季铵类化合物的纳米技术可能是研究和应用的未来发展方向。

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