Controlled Release of Anti-microbial agents for Hospital Acquired Infection

Neeti Srivastava and Rao S Bezwada
Bezwada Biomedical, LLC,
Hillsborough, New Jersey, USA, 08844

Introduction: Hospital acquired infection presents a significant and challenging issue for patients and healthcare providers. The root cause for most of these infections is formation of biofilms on surfaces of medical devices. These medical devices include in dwelling medical devices such as central venous catheters, urinary catheters and reusable medical devices. The work presented in this paper is directed towards developing Triclosan based hydrolysable anti-microbial compounds that can prevent formation of biofilms on surfaces of medical devices.

The anti-bacterial property of triclosan has led to its widespread use in a number of medical devices and consumer products applications. Besides being used in soaps, cleaning agent formulations, anti-microbial fabrics and other consumer articles, formulations containing triclosan have also been used in a number of medical devices including sutures incorporated for extended anti-microbial activity. Inspite of its widespread applications and beneficial anti-microbial properties, the limited solubility of triclosan and related compounds in water renders them non-hydrolysable and reduces their circulation time and hence efficacy at the site of action. Moreover, it is very difficult to polymerize triclosan in its phenolic form. This prevents the beneficial attributes of triclosan and triclosan containing compounds from being used to their full potential.

In this paper, we present for the first time novel hydrolysable triclosan compounds and their macromers. These hydrolysable triclosan compounds and macromers were prepared by functionalization of triclosan with safe and biocompatible molecules such as glycolic acid, lactic acid, p-dioxanone, and/or caprolactone monomers. These monomers are the key components of majority of biodegradable medical devices. This functionalization enhances the native value of triclosan by providing the resultant compound with a specific, controlled degradation profile enabling controlled release of triclosan at the site of action over desired time period. These new functionalized triclosan compounds and macromers have more highly controllable hydrolysis profiles, increased solubility, improved bioavailability, improved efficacy and enhanced functionality.

Synthesis and characterization along with anti-microbial activity of functionalized triclosan compounds and macromers will be presented. *In Vitro* hydrolytic degradation profiles will be discussed.

Results and Discussion: ***Functionalization of Triclosan:*** Triclosan molecule contains a phenolic hydroxyl group as shown in figure 1. In the present study, hydroxyl functional group in triclosan was functionalized with glycolic acid, lactic acid and caprolactone. This functionalization resulted in the formation of novel hydrolysable triclosan compounds. These compounds were then either covalently attached to the biodegradable polymer backbone or were condensed with diols to form dimers. In a similar fashion triclosan molecule was condensed with diacids via esterification to form hydrolysable compounds and dimmers. Representative structures of some of these hydrolysable compounds are shown in figure 2.

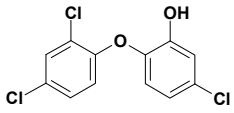

Figure 1. Triclosan

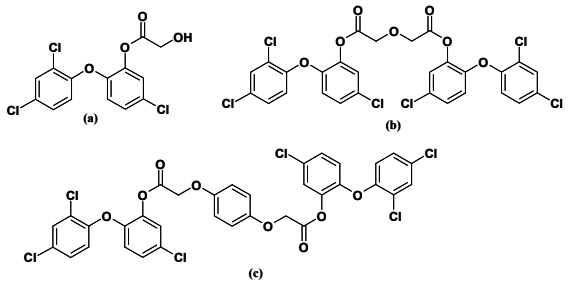

Figure 2. Hydrolysable triclosan based compounds and dimers formed via esterification of triclosan with hydroxyacids and diacids (a) Glycolic acid functionalized triclosan (b) Triclosan diglycolic acid (c) Triclosan hydroquinone diglycolate.

Conclusions: For the first time, novel hydrolysable triclosan compounds and macromers have been prepared. These hydrolysable compounds and macromers not only have a controlled hydrolytic degradation profiles but are also anticipated to degrade into safe and biocompatible molecules. Furthermore, the active portion of functionalized triclosan has improved bioavailability, increased solubility, and better control on degradation rates to provide a targeted delivery of active triclosan component. These novel compounds and macromers will find applications as anti-microbial agents, medical device coatings, cosmetics and controlled release applications, surgical sutures and implantable medical devices.

References: 1. Bezwada, Rao S., US Patent Publication No. 20090105352.