Purified Lipid A can withstand extremes in heat and pressure with its biological activity intact. The core of Lipid A is comprised of B-glucosamine-(1→6)-glucosamine-1-phospho base with fatty acid esters attached to the carbohydrates [4]. It is synthesized by addition of fatty acids and KDO to glucosamine disaccharides. The associated acyl chain groups are largely conserved within a bacterial species and are synthesized in a series of five steps initiated by an acylation step and culminating with a KDO construct that acts as the anchor for the rest of the molecule.

Key words: Endotoxin, Pyrogen, Lipid A, polysaccharide, fever

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Received: January 03, 2018; Accepted: January 21, 2018; Published: January 24, 2018
Biological effects and pathogenicity

Pathogenicity due to the LPS presence is almost entirely due to the Region III component, Lipid A, which in the older literature is referred to as catechin. Overt pathogenicity of Lipid A may initially manifest itself by the development of fever and other changes in metabolism in small doses [4,7]. Body temperature (fever) may rise quickly in individuals infected with lysed Gram-negative bacteria [8]. As Gram-negative bacteria are lysed by the cellular network, the cell walls are broken apart releasing Lipid A to bind with other effector cells such as macrophages. Lethal doses may cause septic shock, hypotension, in addition to fever. Lipid A acts to signal macrophages to produce pyrogens which in turn with activate mediators such as prostaglandins [7, 8, 9]. Prostaglandins act directly on the temperature controls in the brain. The development of symptoms largely depends on the animal species, route of inoculation, dose and timing of systemic release. Binding begins the inflammatory cascade, causing cells to produce and release a variety of cytokines, including IL-1, IL-6, and TNF [7]. The activated cytokine network has multiple and often overlapping effects, including but not limited to complement activation [10,11].

Part of the pathogenicity of Lipid A comes from its' ability to activate the immune system. When Lipid A is detected by cells in the blood cytokines such as TNF and Interleukin 2 are activated [11]. These molecules have a variety of functions including cell activation, complement activation, and stimulation of the release of other cytokines, such as IL-6. These molecules can also be tissue destructive on their own. The cytokines are a major "communication" network among cells and may act very rapidly, especially related to allergic reactions [12].

Summary

LPS is varied and important biological molecule for a variety of reasons, chiefly to human health. The Lipid A component can cause death or shock at the appropriate levels. As such it is important to be able to detect the it not only in the human body but also in the pharmaceutical industry. There are various well published and sensitive techniques for detecting endotoxin in liquids and on medical devices. The major issue with some of these techniques is that they will detect potentially any pyrogen, not just LPS. These organic molecules are often mistakenly referred to as "endotoxin" and may cause a pyrogenic response but are not the integral part of the LPS molecule that Lipid A is part of. Distinctions and an understanding of this fundamental and yet real difference is key to both patient care and pharmaceutical manufacturing.

References