## Polyoxazoline-Conjugated Porcine Serum Albumin as an Artificial Plasma Expander for Dogs

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In modern society, domestic dogs are irreplaceable family members. Veterinary medicine has made tremendous progress, but no adequate supply system exists for their blood products. Hydroxyethyl starch (HES) has often been used as plasma substitute. However, HES causes side effects such as renal dysfunction, blood coagulation disorders, shock, and elevated amylase.<sup>1</sup> In this paper, we report the synthesis, structure, safety, and efficacy of poly(2-ethyl-2-oxazoline)-conjugated porcine serum albumin (POx-PSA) as an artificial plasma expander for dogs.

The POx-PSA was synthesized using a two-step coupling reaction between PSA and unique POx-SH in high yield (**Figure 1**). The average number of POx linked to the albumin was ascertained as 6.0 using MALDI-TOFMS and gravimetric analysis. The secondary structure of the PSA core was retained even after POx binding.

The aqueous POx-PSA solution showed moderately high colloid osmotic pressure and good blood cell compatibility. Actually, lyophilized powder stored for 1 year can regenerate into a homogeneous solution. Neither anti-PSA IgG antibody nor anti-POx IgG antibody were formed in rats. These results contrast to the fact that the injection of polyethylene glycol (PEG)-conjugated PSA (PEG-PSA) generated anti-PSA IgG and anti-PEG IgG antibodies.

Resuscitation of hemorrhagic shock in rats was achieved after injection of POx-PSA solution. The restored mean arterial pressure and heart rates remained constant for 2 hr. Serum biochemistry tests indicated no abnormality in the related organs. These results shows that POx-PSA has potential as an artificial plasma expander for dogs.



Figure 1: Synthetic scheme of POx-PSA.

<sup>1</sup> Myburgh, J. A. et al., N. Engl. J. Med. 2012, 367, 1901–1911.