

What is the optimum concentration of m-cresol in antivenoms?

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Abstract: Antivenoms against snake and scorpion envenomations are usually equine in nature and composed mostly of F(ab')₂; additionally, phenol and m-cresol are mainly employed for their preservation. Although there is no study on this subject, m-cresol is utilized by most manufacturers in a concentration that ranges from 0.15 to 0.35 g%. Decreasing the concentration of m-cresol to its minimal effective level may protect victims from its toxic effects and keep the antivenom stable during its shelf life without forming any aggregates. In the present work, different concentrations of m-cresol, ranging from 0.1 to 0.35 g%, were used with some selected batches of snake and scorpion antivenoms. A low concentration of 0.15 g% showed an acceptable preserving result that complies perfectly with antimicrobial specifications stated by the British Pharmacopoeia. Tested antivenoms (in 12 batches), when kept in a cold room for 39 months (more than their shelf life), retained their physical, chemical and microbiological activities according to the specifications of pharmacopoeias. The present data demonstrated that reduction of m-cresol concentration to 0.15 g% in case of equine F(ab')₂ antivenoms will improve safety of such preparations and preserve their stability during their shelf life.

Key words: antivenoms, preservative, m-cresol, stability.

INTRODUCTION

Antivenoms are refined and concentrated preparations of equine serum globulins – mostly F(ab')₂ – obtained by fractionating blood from healthy horses that were previously immunized with different type of venoms (1, 2). For more than a century, antivenoms have been used effectively as the only treatment for snakebites and envenomations caused by other poisonous animals including spiders and scorpions (3). Most antivenoms are produced in liquid form to lower their cost and ease their use. Currently, there are eight antimicrobial preservatives commonly used in licensed parenteral products of which m-cresol and phenol are habitually employed by manufacturers as preservatives in

antivenom formulations (4-6). Usually, phenol concentrations in antivenoms range from 0.15 to 0.5 g% (7-10). Combinations of phenol and thimerosal in different ratios have also been effectively used in some antivenom preparations (11, 12). M-cresol, a phenol derivative, is frequently utilized as preservative in numerous antivenom preparations in concentrations that range between 0.15 and 0.35 g% (4, 7, 13).

Despite their efficacy as additive, the use of these agents involves the possibility of some adverse effects. It is well known that phenol and cresol are toxic to humans in certain amounts (5, 14-19). Repeated exposure may cause harmful effects on the liver and kidney. Additionally, potential development of multiple organ failure with persistence of organ dysfunction