

Short Communication

Evaluation of Viral Inactivation in Suspension Containing 20% Albumin by Pasteurization Method

Nasiri S^{1*}, Sharifi Z¹

1. Research Center, Iranian Blood Transfusion Organization, Tehran, Iran.

The risks of transmitting viral infections by blood and plasma derived products such as coagulation concentrates immunoglobulin and albumin solutions have long been known and still remain an area of concern (1-8). Emerging pathogens still represent a serious challenge, as demonstrated by West Nile Virus in the US and more recently by chikungunya virus in the Indian Ocean (9). The Pasteurization was the first specific viral inactivation method applied to plasma products. Pasteurization was introduced as early as the 1940s in order to remove the hepatitis virus in the albumin solution (10). To study the efficacy of virus inactivation during pasteurization, albumin solution 20% vials were spiked with model viruses such as HSV-1 and polio virus type 1 as enveloped and non-enveloped viruses respectively. Virus stock titers were 1×10^6 TCID₅₀/mL (tissue culture infectious dose 50% per ml) for HSV-1 and $1 \times 10^{6.5}$ TCID₅₀/mL for polio virus in Vero cell culture. The virus-spiked albumin solutions were treated by heating at 60 °C for 10 hr. Viral infectivity was tested in cell culture (Vero) using standard micro titration assay (11). Seventy two hours after inoculation, virus-induced cytopathic effect was scored and infectivity titers were calculated according to the Reed and Muench Method and expressed as log₁₀ TCID₅₀/ml. The inactivation kinetics of HSV-1 and

poliovirus type-1 as model viruses by pasteurization were investigated. Results are shown in figures 1 and 2.

It was observed that HSV-1 and poliovirus type-1 were completely inactivated within one and two hours respectively. The reduction factors after the full ten hours period were at least 6 log for HSV-1 and 6.5 log for poliovirus respectively. The assays were performed duplicated with non-heated controls. We didn't find any significant virus reduction in non-heated controls. The rate of inactivation of poliovirus was slightly slower than herpes simplex virus. It has been shown that Encephalomyocarditis virus as a model virus (non- enveloped) can be inactivated 4 log in less than 30 min during albumin pasteurization (12). In another study it was reported that in caprylate stabilized albumin solution, herpes simplex virus was inactivated more than 7.2 log in 30 min (13). Also, the results of this study indicated that pasteurization for 10 hr can reduce HSV-1 titer to about 6 log and of poliovirus to about 6.5 log. On the other hand, our previous study showed that pasteurization method can inactivate 5.8 log of HSV-1 and 6.3 log of poliovirus in human coagulation factor VII concentrate (70% sucrose, 20% glycine) in 6 and 8 h respectively (14). These findings indicate that application of pasteurization method for human serum albumin is more efficient than using it for other plasma products and can increase the safety of albumin products.

*Corresponding author: Saleh Nasiri, Ph.D,
Research Center of Iranian Blood Transfusion
Organization (IBTO), Tehran, Iran.
Tel: (+98) 21 88 60 15 01 30, Fax: (+98) 21 88 60 15
55
Email: snasiri2002@yahoo.com

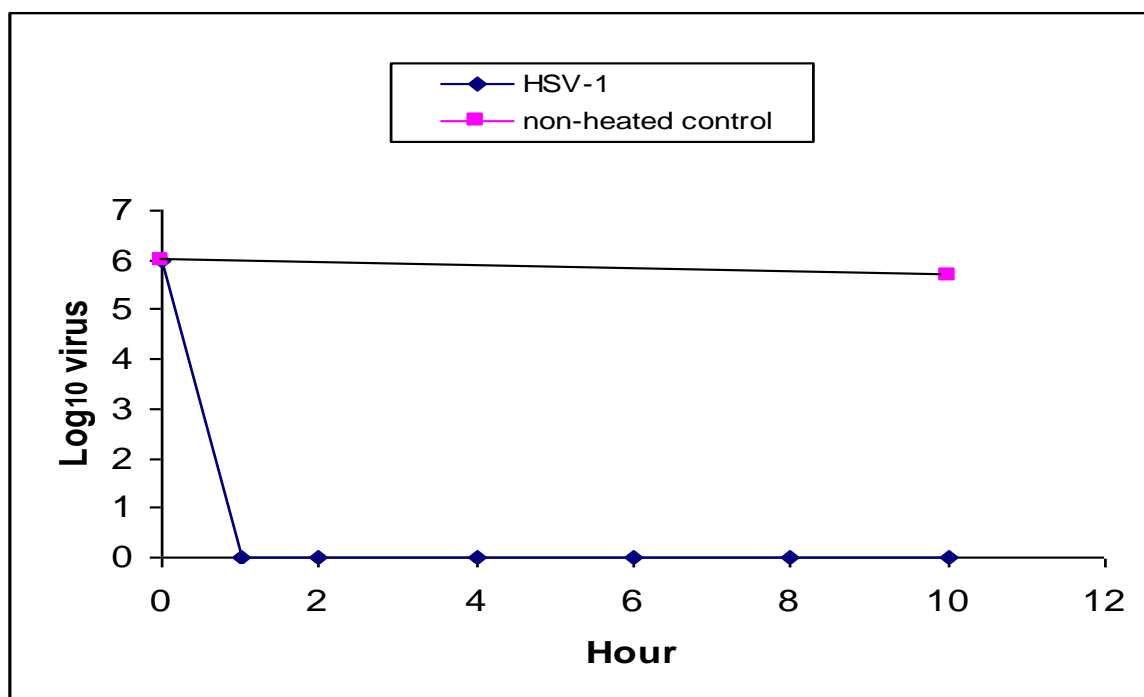


Fig. 1. Rate of herpes simplex virus inactivation on pasteurization of 20% albumin at 60° C for 10 hours.

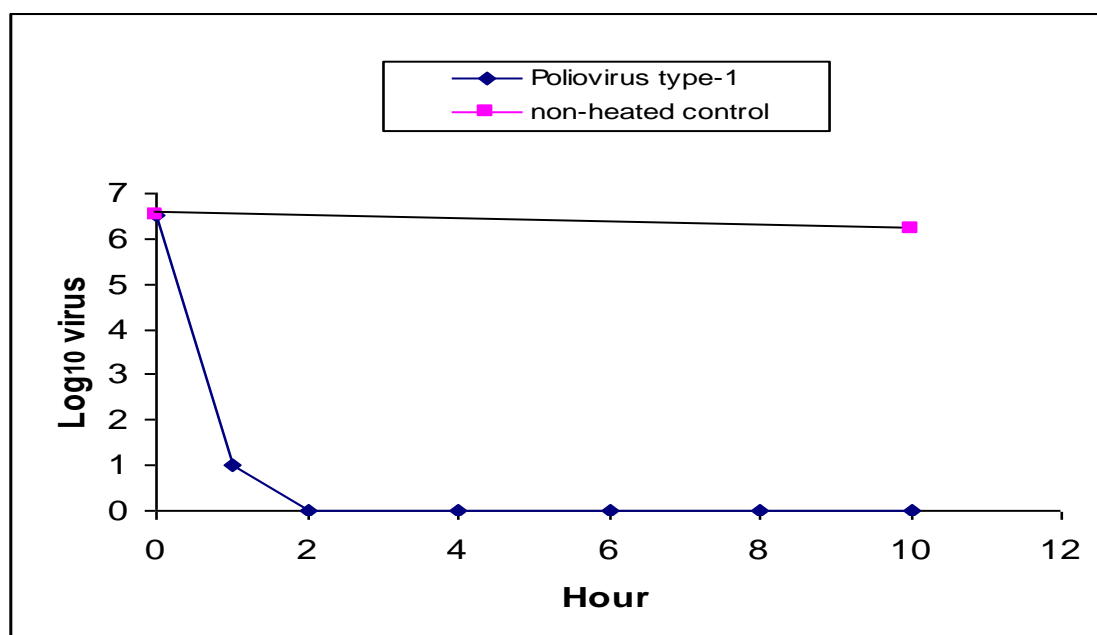


Fig. 2. Rate of poliovirus inactivation on pasteurization of 20% albumin at 60° C for 10 hours.

References

1. Prince AM, Horowitz B, Horowitz MS, and Zang E. The development of virus-free labile blood derivatives: a review. *Eur J Epidemiol.* 1987; 2: 103-18.
2. Thomas D. Viral contamination of blood products. *Lancet.* 1994; 343: 1583-4.
3. Roberts P. Virus safety of plasma products. *Rev Med Virol.* 1996; 6: 25-38.

4. Burnouf T. Viral safety of plasma products – do we have zero risk? *Transfusion and Apheresis Science*. 2001; 24:139.
5. Kreil T. R, Unger U, Orth S.M, Petutschnig G, Kistner O, Poelsler G, and Berting A. H5N1 influenza virus and the safety of plasma products. *Transfusion* 2007; 47: 452-459.
6. Fryer JF, Hubbard AR, and Baylis SA. Human parvovirus PARV4 in clotting factor concentrates. *Vox Sang*. 2007; 93: 341-347.
7. Mpandi M, Schmutz P, Legrand E, Duc R, Geinoz J, Henzelin-Nkubana C, et al. Partitioning and inactivation of viruses by the caprylic acid precipitation followed by a terminal pasteurization in the manufacturing process of horse immunoglobulins. *Biologicals*. 2007; 35:335-41.
8. Barin F. Viral safety of biologicals. *Ann Pharm Fr*. 2008; 66:129-139.
9. Solheim BG. Pathogen reduction of blood components. *Transfus Apher Sci*. 2008; 39: 75-82.
10. Edsall JT. Stabilization of serum albumin to heat , and inactivation of the hepatitis virus. *Vox Sang*. 1984; 46: 338-340.
11. Hierholzer JC, and Killington RA. Virus isolation and quantitation. In: Mahy BWJ, Kangro HO, eds . *Virology Methods Manual*. London: Academic Press Ltd; 1996; 25-46.
12. Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products. WHO Technical Report Series. 2004; 924:150-224.
13. Global blood safety initiative: viral inactivation of blood and blood products. WHO Publications, 1992; 5: 1-33.
14. Rezvan H, Nasiri S, and Mousavi K. Inactivation of poliovirus type-1 and HSV-1 in human coagulation factor VII concentrate by pasteurization. *Archives of Iranian Medicine*. 2001; 14: 10-13.