Manufacturing of viral vaccines

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Abstract

Background:
Viral vaccine contain inactivated viruses or live viruses.Viral diseases still cause human deaths in the endemic areas in Asia and Africa. A cheap vaccine for human, that could be used in mass vaccination campaigns, would be a valuable weapon against viral diseases. Serum institute of India Pvt Ltd has developed several vaccines such as Rabies, Corona (Covishield), Polio, Measles, Mumps, Rubella, Rota vaccines.

Methodology, theoretical orientation and Findings:

Example: Rabies Vaccine Manufacturing Process

Large scale production of Vero ATCC CCL81 cells were seeded in Cell cube system / bioreactor. Then cells are infected with Pitman Moore (PM 3218) strain of rabies virus. After 48-72 hrs infected cells are washed. The multiple harvests are collected from cell cube system / bioreactor, which is then clarified by filtration. Clarified harvest is concentrated using tangential flow filtration system. Inactivation of rabies virus is done using beta-propiolactone (BPL).

Next step of purification is done by affinity column chromatography in order to remove BSA, host cell DNA host cell protein and diafiltration to remove high salt concentration. Purified rabies antigen is prepared by adding stabilizer to diafiltered antigen and finally filtered by 0.2-micron filtration then stored in ethyl vinyl acetate bags. The purified rabies antigen and blind vaccine if requires blend to achieve set antigen content in final bulk. The liquid vaccine is filled in 1 ml USP type 1 clear and tubular vial and lyophilized. With the lyophilized vial of rabies vaccine 1.0 ml of sterile water for injection is supplied as a diluent.
Conclusion and significance:

Diseases can be eliminated and eradicated by using vaccines such as MMR, Rabies, Corona (Covishield), Polio and Rota. Study of Rabies gives well- developed new purified Vero cell rabies vaccine (Rabivax-S), following all the GMP requirements. Animal study has demonstrated no toxicity issue. We evaluated its safety, toxicity and immunogenicity in post-exposure prophylaxis in clinical trials by IM and ID routes. vaccine is good option among the available modern WHO prequalified rabies vaccine. The preparation of purified rabies antigen is proceed in a stepwise manner with the large-scale production of Vero cells, rabies virus propagation, virus inactivation, purification of inactivated antigen and antigen stabilization. Initially low passage of vero cells is revived.Large-scale production of Vero ATCC CCL81 cells were seeded in CellCube system. Then cells are infected with Pitman Moore (PM3218) strain of rabies virus. After 48-72 hrs of incubation infected cells are washed. The multiple harvests are collected from one Cell Cube system and clarified by filtration. Clarified harvest is then concentrated using tangential flow filtration system to reduce working volume of live rabies virus for further processing. Inactivation of rabies virus is done using beta-propiolactone (BPL). In the next step, purification is done by affinity column chromatography with cellufine sulfate resin in order to remove BSA, host cell DNA and host cell protein. The column-eluted antigen is diafiltered by TFF system to remove high salt concentration. Purified rabies antigen is then prepared by adding stabilizer to diafiltered antigen in 1:1 v/v ratio. Finally, antigen is filtered by 0.22-micron filter and collected in media bags. These bags then stored at 2- 8°C.

Results and Discussion
Study gives well-developed new purified vero cell rabies vaccine, following all the GMP requirements. This vaccine is good option among the available modern WHO pre-qualified rabies vaccine.
The new things about Rabies vaccine is that the PM 3218 strain was for the first time successfully adapted on Vero ATCC CCL 81. The adaptation worked very well. Rabies virus is inactivated by using BPL at 1:3500 at 2 to 8°C within 24 hours after addition of BPL. During purification optimal reduction in HCP, residual DNA, BSAand other impurities is observed. Study also gives optimal recovery of rabies glycoprotein during purification process.

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