IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2020 Vol.:19, Issue:1

Storage Conditions and Stability of Official Vaccines

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Maruthi Valluru

Associate Prof, Faculty Of Pharmaceutical Sciences, VJS College of Pharmacy, Rajahmundry. A.P., India

Submission: 21 July 2020
Accepted: 28 July 2020
Published: 30 August 2020

Keywords: Immunity, Vaccine, Toxoid, Antigen, Polyvalent

ABSTRACT

Vaccines are preparations of antigenic materials, which are administered with the objective of including in the recipient and active immunity against the infectious microorganisms or toxins produced by them. They may contain living or killed microorganisms, bacterial toxoids or antigenic from particular parts of the bacterium, rickettsia or virus. Unlike chemical drugs, many biological preparations are unstable during storage and this instability can reduce the safety and efficacy of the biological medicinal product.

HUMAN JOURNALS
www.ijppr.humanjournals.com

INTRODUCTION

Vaccines or sera are biological products which act by reinforcing the immunological defence of the body against foreign agencies (infecting organisms or their toxins). The agents or products through which immunization is achieved are called immunizing agents. Active immunisation is the process of increasing resistance to infections whereby microorganisms or products of their activity act as antigen and stimulates certain body cells to produce antibodies with a specific protective capacity. Biological products comprising vaccines and toxoids confer active immunity. Passive immunisation which results in immediate protection of short duration, may be achieved by the administration of antibodies themselves. Biological products comprising human immune sera and animal immune sera confer passive immunity. These immunological preparations are classified. Vaccines and sera are potentially dangerous products and mostly used in public health programmes. These biological are standardised by bioassays and stored in a cold place to maintain potency.

Classification of various vaccines

Vaccines may be single-component or mixed component vaccines. Single vaccines are prepared from a single species of microorganisms. Mixed or compound vaccines are prepared from two or more species. Simple vaccines containing only one strain of a species are univalent and those containing two strains of the same are called polyvalent.

Live attenuated vaccines: Live attenuated vaccines consist of live bacteria or viruses which have been rendered avirulent e.g. B.C.G vaccine, smallpox.

Killed vaccines: Killed vaccines are suspensions of bacteria or of viruses that have been killed by heat or by disinfectants such as phenol or formaldehyde. The best known vaccines are pertusis, cholera, plague, influenza and rabies vaccine.

Bacterial cell component vaccine: Some bacterial vaccines do not contain whole bacterial cells but contain components of bacterial cell. Such vaccines induce a response that is more specific and effective e.g. Haemophilus influenza Type B vaccine, Neisseria meningitidis Type A and C.

Viral subunit vaccines: The influenza vaccines are prepared by treating intact influenza virus particles from embryonated hens eggs, infected with influenza virus with a surface

acting agent. The virus particles are disrupted and release the viral subunits, haemagglutinin and neuraminidase that are required in the vaccine. Another example of viral subunit vaccine is hepatitis B vaccine.

Preparation of vaccines (General methods)

The starting stage for the preparation of all microbial vaccines is the isolation of suitable microbial strains are mainly isolated from human infections and in some cases have required elaborate laboratory manipulation and selection. Once a suitable strain is selected, a sizeable culture is prepared. This culture is called 'seed lot'. The biological properties of seed material are carefully examined in the laboratory. The seed is then used to make one or more batches of vaccine production. If it is found satisfactory, then it is tested for efficacy and safety in clinical trials. Satisfactory results in the clinical trials validate the seed lot and it is used for production of vaccines.

Preparation of viral vaccines

Virus replicates only in living cells, hence the first viral vaccines against smallpox and rabies were made in intact mammalian hosts (calves, sheeps, rabbits). Today, the only intact host used in advanced production techniques is the developing chick embryo. Almost all virus growth is preferably achieved in cell cultures. The chick embryo is the most convenient host for the growth of viruses that are needed for influenza and yellow fever vaccines. Influenza viruses accumulate in high titre in the allontoic fluid of the eggs and yellow fever virus accumulate in the nervous systems of the embryos.

Different techniques are used for the processing of viral materials. Allantoic fluid is centrifuged to provide a concentrated and partially purified suspension of influenza virus. This concentrated and partially purified suspension of influenza virus is treated with either or other agents to split the virus into its components. Cell cultures provide infected fluids that contain little debris and that can be separated by filtration. Most viral vaccines are not inactivated because they are made from cultures consisting of live attenuated virus. But inactivated poliomyelitis virus vaccine is inactivated with dilute formalin or β-propiolactone, and rabies vaccine is inactivated with β-propiolactone. When processing is complete, the bulk materials may be stored at -70ºC until needed for blending into a final vaccine.

Blending of vaccines

Blending is the process in which the various components of a vaccine are mixed to form a bulk. A single component final bulk is prepared by adding bacterial suspension or bacterial components e.g. BCG vaccine, cholera vaccine, diphtheria vaccines *etc*. A multiple component final bulk of a combined vaccine is made by adding each required component e.g DTP vaccine (in bacterial toxoids). These vaccines blended with an adjuvant are called 'plain vaccines' or 'fluid' vaccines (in bacterial toxoids). Those vaccines blended with an adjuvant (e.g. aluminium hydroxide) are called adsorbed vaccines preservatives (thiomersal) are added in killed bacterial vaccines in multidose containers.

When viral vaccines are blended, it is necessary to maintain adequate antigenicity or infectivity. After proper mixing, a final bulk may be separated into a number of small size containers to facilities handling e.g. measles vaccine, poliomyelitis vaccine, rabies vaccine, smallpox vaccine *etc*. Live attenuated viral vaccines lose potency in the suspension hence, these vaccines are stored at low temperatures or a stabiliser may be added. Live attenuated viral vaccines lose potency in the suspension hence, these vaccines are stored at low temperature or a stabiliser may be added. Live attenuated poliomyelitis vaccines is stabilised by using magnesium chloride or sucrose.

Quality control of vaccines

The quality control of vaccines is intended to provide assurances of efficacy and safety. Quality of vaccines is checked in two ways in process control and final product control.

In process control:

In process quality control is the control exercised over starting materials and intermediates. The quality control of diphtheria and tetanus vaccines requires that the products are tested for the presence of free toxins. Adequate infectivity of the virus from the tissue cultures is an indicator of the adequate virus content of the starting materials and since infectivity is destroyed in the inactivation process. In case of tissue culture substrates, exclude contamination with infectious agents from the source animal or in the case of human for simian herpes B virus, simian virus 40 and mycoplasmas.

Final product control is the quality control exercised by the monographs of a pharmacopoeia over products in their final containers. All vaccines are tested for identity, potency and safety, combined vaccines are required to pass tests prescribed for each of the separate components.

Identification tests for vaccines

The identities of bacterial vaccines can be checked by precipitation and agglutination reactions. Inactivation viral vaccines are tested by observation of the specific antibody responses in vaccinated animals and live viral vaccines by neutralisation of their cytopathic effects by specific antisera.

Potency assay

Vaccines containing killed microbes or their products are tested for potency in which the amount of the vaccine that is required to protect animals from a defined challenge dose of the pathogen. The potency whooping cough vaccine is estimated by 3+3dose quantal assay method as per pharmacopeia. Three logarithmic serial doses of the test vaccine and three logarithmic serial doses of the standard vaccines are inoculated each in a group of 16 mice. On the basis of experience, a middle dose of test and standard that induce a protective response in about 50% of the animals are selected. Fourteen days later all of the mice are infected with *Bordetella pertusis* and after a further 14 days, the number of mice surviving in each of the six groups are counted the number of survivors in each group are then used to calculate the potency of the test vaccine relative to the standard vaccine. Same tests may be used for the estimation of the potencies of diphtheria and tetanus vaccines. Vaccines containing live microorganisms are generally tested for potency by counts of their viable cells e.g. BCG vaccine. The potency of live viral vaccines is estimated by using substrates of living cells. Dilutions of vaccines are inoculated on the tissue culture monolayers in Petri dishes and the live count of the vaccines is calculated from the infectivity of the dilutions and dilution factor involved. Potency of many vaccines is also checked by physic-chemical or serological techniques.

Safety tests

Viral vaccines have some problems for activity testing as compared to bacterial vaccines. Killed bacterial vaccines must be completely free from living microbes used in the production process. The final product must provide an assurance that all microorganisms

have been killed. Incomplete virus inactivation is detected by inoculation of susceptible tissue cultures and of susceptible animals. The cultures are examined for cytipathic effects and the animals for symptoms of disease.

Sterility test

All vaccines must be bacteriologically and mycologically sterile. In each batch of a product the number of containers to be tested depends on the batch size and is the subject of pharmacopoeial regulation. Membrane filtration method is commonly used for sterility testing of vaccines.

Free formalin testing

Inactivation of bacterial toxins by formalin may lead to the presence of free formalin in the final product. The concentration of free formalin may not exceed 0.02% which is estimated by colour development with acetylacetone.

Abnormal toxicity testing

This test is used for detection of toxic contamination in vaccines. Five mice (approx 20gm) and two guinea pigs (approx 300gm) are inoculated with one human dose or 1.0ml (whichever is less) of the test preparation. All must survive for 7 days without sign of illness.

Phenol concentration

Phenol is used as a preservative in different types of vaccines. Its concentration must not exceed 0.5%w/v.

Presence of aluminium and calcium

Aluminium hydroxide, aluminium phosphate and calcium phosphate are commonly used in vaccines as an adjuvant. The quantity of aluminium must not exceed 1.25mg/dose and is estimated complexiметrically. The quality of calcium must not exceed 1.3mg/dose and is usually estimated by flame photometry.

Storage of immunological products

Preservation of the potency of immunological products involves maintaining the viability of living cells or preventing the denaturation of proteins. Most vaccines and immunological

preparations are stored at low 2 to 10ºC. Viral vaccines (e.g. smallpox and oral poliomyelitis) are more stable at or below their freezing points but bacterial vaccines or antitoxins are easily deteriorated if they are allowed to freeze. This may be due to mechanical damage by ice crystals or the adverse effects of inorganic salts. Freeze dried vaccines are stable as compared with corresponding liquid forms. Freeze dried smallpox and yellow fever vaccines must be kept at not more than 10ºC and 0ºC respectively.

Immunological products must be protected from light because these products usually accelerate decomposition in presence of light. Dilution and the choice of diluents may also influence stability. The diagnostic preparations, undiluted old tuberculin, are stable for 8 years good stock control is particularly important for biological preparations.

Immunological products must protect from because these products usually accelerate decomposition in presence of light. Dilution and the choice of diluent may also, but when diluted, its stability depends on the degree of dilution and the nature of diluent. Good stock control is particularly important for biological preparation.

CONCLUSION

The present study clearly showed the need for continuous education on storage and Good vaccine practice by both physicians and health care professionals, and other personnel in general and vaccine storage management in particular. In vaccine medication, the correct storage of vaccines is crucial since both too low and too high temperatures can provoke damage to specific vaccine types. Adjuvant killed or subunit vaccines can be damaged (e.g. structure of aluminium hydroxide in adjuvatns) by too low temperatures (below 0 °C), whereas lyophilized live vaccines are susceptible (e.g. loss of vaccine potency) to heat damage by temperatures above +8 °C. In conclusion, knowledge and awareness of Good vaccine practice and vaccine storage conditions are crucial under practical field conditions in vaccination of paediatrics. Focus on correct vaccine storage is part of the responsibility of health care professionals in order to obtain the required vaccine efficacy.

REFERENCES:

1. Rawlins E.A.,(ed),(1992). Bentleys Textbook of Pharmaceutics, English Edition, Bailliere Tindall, London.
2. Kokare C.R, (2007) Pharmaceutical Microbiology – Experiments and Techniques, Second Edition, Career Publications, Nashik, India.
3. Lorian V. (1986). Antibiotics in Laboratory Medicine. Second Edition, Williams and Wilkins. Co. Baltimore, USA.

4. Ketchum P.A (1988). Microbiology-concepts and applications, John Wiley and Sons, New York.
5. Heritage J. *et al.* (1996). Introductory Microbiology, First Edition, Cambridge University Press.
6. Ingraham J.L and Ingraham C.A (2000). Introduction to Microbiology. Second edition. Thomson Books/cole.
7. Rehm H.J and Reed G (eds). (1989). Biotechnology, Volume 7b, VCH Publishers.
8. Talaro K and Talaro A (1996). Foundations in Microbiology, Second Edition. Wm C Brown
9. Winfeild A.J and Richards R.M.E (eds), (1998). Pharmaceutical practice, Second Edition, Varghese Publishing House.
10. Stites D.P, *et al*. (ends), (1994), Basic and clinical immunology, English Edition, Practice-Hall international Inc.