Introduction
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The strategy of World Health Organization (WHO) is to develop efficient and inexpensive vaccine against various diseases. In 1974, the World Health Organization officially launched a global immunization programme called Expanded Programme on Immunization (EPI). The ultimate aim of EPI was to protect all children of the world against vaccine preventable diseases specifically diphtheria, whooping cough, tetanus, polio, tuberculosis and measles by the year 2000. The high proportion of chronic infection that is acquired during childhood can be prevented by routine infant immunization programme. The Expanded Programme on Immunization is now called Universal Immunization Programme (UIP). The EPI was launched in India in 1978 after successful global eradication of small pox in 1975 through effective vaccination programmes and strengthened surveillance. Vaccine development and immunization constitute critical component of the public health policy in any country. Accordingly, the Global Programme for Vaccines and Immunization (GPV) were established in 1994. The programme thus has terms of orientation that span from vaccine research, through vaccine production and quality control to help ministries of health plan and manage their immunization services to control vaccine preventable diseases. The Children's Vaccine Initiative (CVI) is a companion organization to the Global Programme for Vaccines and Immunization and has its own strategic plan. The purpose of CVI is to develop new technologies to progress and develop single dose efficient vaccine. It should be given as a single dose (preferably orally), effective when administered near birth, heat stable, contain multiple antigens and effective against diseases. With a particular focus on the world's poorest children, GPV aims at strengthening routine immunization services, increasing coverage and introducing
new vaccines. The three main objectives of the Global Programme are self-sufficiency, disease control and production of new vaccines.

1. **Self-sufficiency**

   All countries should become self-sufficient in their immunization programmes. This means that the country should be independent of outside support for funding, management, technical assistance, vaccine supply, equipment, and training.

2. **Disease control**

   All vaccine-preventable diseases included in the programme are monitored and controlled to a point where they are eradicated, eliminated, or cease to be a public health problem.

3. **New vaccines**

   New and improved vaccines are made available to the public as soon as science, resources, and national programme management will allow.

   Global Alliance for Vaccines and Immunization (GAVI), an advisory group comprising National Governments and International agencies such as WHO, World Bank, UNICEF and industries was launched on January, 2000. GAVI’s mission statement is “To save children’s lives and protect people’s health through widespread use of vaccines with a particular emphasis on developing countries”. The main objectives of GAVI are

   1. Improve access to sustainable immunization services
   2. Expand use of all existing cost–effective vaccines
   3. Step up to introduce new vaccines
   4. Accelerate vaccine research and development for diseases particular importance to developing countries
5. Make immunization coverage a focus in the design and assessment of international development efforts.

The GAVI Alliance (formerly known as GAVI) is a public–private partnership focused on increasing children’s access to vaccines in poor countries. As an alliance of major leaders in international health and development, GAVI has great potential to effect decision making among policy makers and donors on the value of vaccination for reducing poverty and infant mortality in the developing countries. Through the GAVI fund, the alliance provides financial resources to countries to purchase vaccines and to support immunization. The global advisory group of the Expanded Programme on Immunization of WHO in 1991 recommended that by the year 1997, hepatitis B vaccine should be introduced into national immunization programme in all countries. Accordingly, hepatitis B vaccine has been included under National Immunization Programme of more than 130 countries. Numerous studies have reported that adding hepatitis B vaccine into EPI is highly cost effective, even in areas with low HBV endemicity. Most of the serious consequences of HBV infections (i.e. liver cancer and cirrhosis) occur among persons who are chronically infected and serve as main reservoir for the transmission of new infections.

The principal objective of hepatitis B immunization strategies is therefore to prevent chronic HBV infections. Hepatitis B is an acute systemic infection, which turn into a major public health problem all over the world. Hepatitis B virus infection can lead to fulminant hepatic failure (FHF), which acutely threatens the life of affected patients (Ludger Leifeld et al., 2002). Approximately 30% of world’s population has serological evidence of hepatitis B virus infection (Kane, 1996). It is estimated that 350 million of them are chronic hepatitis B infected, about a million of which die every year from chronic liver disease, including cirrhosis and liver cancer.
Hepatitis B infection is an important cause of morbidity and mortality after kidney transplantations (Pirson et al, 1977; Parfrey et al, 1985; Harnett et al, 1987; Rao et al, 1991 & Philippe Mathurin et al, 1999). Progressive liver disease affects more than 80% of HBsAg positive renal transplant recipients. Hepatitis B virus is the major cause of hepatocellular carcinoma worldwide next to tobacco a known human carcinogen (Joseph Torresi and Stephen Locarnini, Gastroenterology, 2000). The liver disease associated with hepatitis B infection results largely from the immune response to the virus. In seeking to kill the virus, the immune system damages the liver cells due to viral multiplication. Chronically infected persons are called carriers and are affected by cirrhosis and liver cancer (Robert Perrillo, 2001 and Moyer, 1994). In the United States, an estimated 3000 to 4000 persons die of HBV related cirrhosis and 1000 to 1500 persons die of HBV related liver cancer each year. Even though individuals with chronic HBV infection may be asymptomatic and unaware that they are infected, they are capable of infecting others. Chronic liver disease is particularly likely to occur in patients who remain seropositive for HBsAg and who become super infected with the hepatitis D virus. The diagnosis of acute hepatitis B infection is confirmed by detection of the surface antigen and IgM antibody to the core antigen. The presence of HBeAg is indicative of an exceptionally high inoculum and active viral replication. Patients with chronic hepatits B infection have persistence of the surface antigen in the serum and liver tissue. Development of anti HBs (antibody to Hep B surface antigen) indicates immunologic response to infection.

The HBsAg is highly immunogenic and induces anti HBs (humoral immunity). Structural viral proteins induce specific T - lymphocytes, capable of eliminating HBV infected cells by cellular immunity (Arie Zuckerman, 2000). HBsAg is heterogenous antigenically, with a common antigen esignated a and two pairs of
mutually exclusive antigens d and y; and w and r designated to nominate 4 major subtypes adw, ayw, adr and ayr.

Transmission

HBV is spread by either skin puncture or mucous membrane contact with infected blood or other body fluids. The highest concentration of virus occurs in blood and wound secretions. Moderate concentration of HBV is found in semen and vaginal fluid, and lower concentrations occur in saliva (Robinson, 1994 and 1995). HBV is not spread by air, food, water and faeces.

The primary routes of spread are
1. Perinatal transmission
2. From child to child
3. Through unsafe injections and blood transfusions
4. Through sexual contacts

1. Perinatal transmission

Perinatal transmission from mothers infected with HBV i.e. positive for HBsAg, to their new born infants is a major source of HBV infection in many countries (Margolis et al, 1995; Vivian Wong et al, 1984; Zhi-Yi Xu et al, 1985; Stevens et al, 1987; Poovorawan et al, 1989; Beasley et al, 1983 and Lee et al, 1991). Perinatal transmission occurs predominantly due to the infant exposure to infected blood and genital secretions during delivery. In the absence of immunoprophylaxis for the neonate, perinatal transmission occurs in 10 - 20 %, who are seropositive for HBsAg. The incidence of perinatal transmission increases to almost 90 % in women, who are seropositive for both HBsAg and HBeAg (Deinhardt, 1982). The mechanism of perinatal infection is still uncertain. HBV can infect the foetus in uterus. This rarely happens and most infections appear to occur at birth as a result of leak of maternal
blood into baby’s circulation or ingestion or accidental inoculation of blood (James Hill et al, 2002). Breast feeding has been recommended as an additional mechanism by which infants may acquire HBV infection, because small amounts of Hepatitis B surface antigen (HBsAg) have been detected in some samples of breast milk. There is no evidence that breast feeding increases the risk of mother to child transmission. However, cracked or bleeding nipples or lesions with serous exudates could cause hepatitis B. The risk of perinatal transmission depends on the presence of HBe antigen in the blood of mothers infected with HBV. The risk of chronic HBV infection is in the approximate range 70 – 90 % from such mothers, who are HBeAg positive and about 5 – 20 % from those who are HBeAg negative (Okada et al, 1976; Palmer Beasley et al, 1977 and Gust, 1996) The risk for babies to be infected by HBsAg positive mothers varies from country to country and is closely related to the proportion of women of child bearing age for HBsAg.

2. Child to child transmission

The spread of HBV from child to child accounts for most HBV infection (Simonsen et al, 1999; Kane et al, 1999 and Alter and Margolis, 1990). Transmissions usually happen in household settings but may also occur in child day care centers and in schools (Arie Zuckerman, 2000). The most probable mechanism of child to child spread involve contact of skin sores, small breaks in the skin or mucous membrane with blood or skin sore secretions (Philippe Mathurin et al, 1999). HBV may also spread because of contact with saliva through bites or other bites or other breaks in the skin, and as a consequence of the premastication of food (Robinson, 1994 and 1995; Margolis et al, 1995). In addition the virus may spread from inanimate objects such as shared towels or tooth brushes, since it can survive for at least seven days outside the body and can be found in titres on objects even in the

3. Transmission associated with injection and blood transfusion

In many countries unsafe injection practices are major source of transmission of HBV and other blood born pathogens (Simonsen et al, 1999 and Kane et al, 1999). Blood transfusion is a chief source of HBV transmission in countries, where the blood supply is not screened for HBsAg. Many developing countries, up to 50% of injections are administered with needles and syringes that are reused without sterilization. Substandard infection control practices, including the reuse of contaminated medical or dental equipments, failure to use appropriate disinfection and sterilization for equipment, environmental surfaces, and improper use of multidose medication vials can also result in the transmission of HBV and other blood borne pathogens. In addition, the injection of prohibited drugs and tattooing with unsterilized needles are common modes of HBV transmission in many countries.

4. Sexual transmission

HBV is efficiently transmitted by sexual contact, which can account for high proportion of new hepatitis B among adolescents and adults in countries with low and intermediate endemicity of chronic HBV infections (Alter and Margolis, 1990). Sexual intercourse especially anal sex and homo sex with an infected partner are known to be important risk factors for transmission of HBV. Studies have shown that 16-40% of sexual partners of individuals with clinical or sub clinical chronic hepatitis B will acquire the infection. HBV is not transmitted by casual contact such as touching, hugging, or kissing unless blood-to-blood or saliva-to-blood contact is possible, eg, through a cut lip or bleeding gums.
Epidemiology

The Hepatitis B virus is present worldwide and has infected more than 2000 million people. The United Kingdom and the United States of America have a low prevalence but it rises to 10 - 15 % in some parts of Africa. The prevalence of HBV infection varies markedly throughout regions of the world. Hepatitis B is highly endemic in developing countries with large population such as South East Asia, China, sub-Saharan Africa and the Amazon Basin, where at least 8% of the population are HBV chronic carriers. Approximately 45% of the world population live in areas where chronic HBV infection is highly endemic (≥ 8% of the population are HBsAg-positive) 43% live in areas of intermediate endemivity (2-7% HBsAg-positive) and 12% live in areas of low endemity (≤ 2% HBsAg-positive). In areas of high endemivity the life time risk of HBV infection is more than 60% and the majority of infections are acquired from perinatal and child to child transmission. When the risk of developing chronic infection is the greatest in these areas, acute hepatitis B is uncommon because most perinatal and early childhood infections are asymptomatic. However, rates of liver cancer and cirrhosis in adults are very high. Hepatitis B is moderately endemic in part of Eastern and Southern Europe, the Middle East, Japan, and part of South America. Between 10–60% of the population have evidence of infection, and 2-7% is chronic carriers. Acute disease related to HBV is common in these areas because many infections occur in adolescents and adults. However, the high rates of chronic infection are maintained mostly by infections occurring in infants and children. In these areas, mixed patterns of transmission exist, including infant, early childhood and adult transmission. However, high rates of chronic infection are maintained mainly because of infections occurring infants and children (Toukan, 1990). In areas of low endemity the life time risk of HBV
infection is less than 20%. The endemicity of HBV is low in most developed areas such as North America, Northern and Western Europe and Australia. In these regions, HBV infects 5–7% of the population, and only 0.5–2% of the population is chronic carriers. In these areas, most HBV infections occur in adolescents and young adults in relatively well-defined high-risk groups, including health care workers, injection drug user, homosexual males, patients who require regular blood transfusion or hemodialysis (Geraldine McQuillan et al, 1989). India is the most densely populated country in Asia and the second most populous country in the world. However, India still faces enormous public health problem especially due to hepatitis B. In hyper endemic countries, the age specific prevalence of markers of infection increases steadily with increasing age. In these countries the most important mode of transmission of HBV infection is perinatal, when newborn babies are exposed to the infected blood or blood stained secretions of carrier mothers. However, horizontal transmission from family members plays a key role in the spread of HBV.

**Hepatocellular carcinoma (HCC)**

Hepatocellular carcinoma affects approximately half a million persons every year worldwide. Carriers of HBV and HCV have extremely high risk in developing HCC. In areas where HBV is prevalent, 90% of patients with liver cancer are due to HBV infection. Hepatocellular carcinoma is uncommon in Europe and North America but worldwide it is the commonest cause of death from malignancy. In areas such as Sub-Saharan Africa and Southeast Asia (and especially Taiwan and China) HCC is the most common cancer, generally affecting men more than women. This variability is in part due to the different patterns of hepatitis B transmission in different populations - infection at or around birth (as in Taiwan) predispose to earlier cancers than if people are infected later. In India, population based studies have been
established by Indian council of Medical Research in Chennai, Bangalore, Bhopal, Delhi and Mumbi. It has been estimated that approximately 11000 to 12500 of liver cancer occur every year in India.

**Status of current treatment and vaccines for hepatitis B**

There is no specific treatment eventhough certain drugs like interferon- α and lamivudine are climbed to cure hepatitis B. However, the magnitude of these drugs (interferon α and lamivudine) varies from person to person and responds to certain patients only (Lok et al, 1992; Graeme Alexander et al, 1987 and Hoofnagle et al, 1998). In spite of these drawbacks, vaccination is the only way to alter disease prevalence. Therefore, vaccination is the only way to prevent hepatitis B infection. Prevention also depends on avoiding risk factors such as shared needles, multiple male homosexual partners and prostitutes. A safe and effective vaccine against hepatitis B virus infection has been made available for nearly 20 years. However, it requires three doses that must be given at 0, 1st, and 6th month soon after birth to elicit an optimum immune response. Besides, the immune response gradually declines with increasing age and repeated immunizations may result in seroconversions. Moreover, the cost of vaccine and immunization schedule is deterrent to global immunization programme to combat hepatitis B.

**Current status of immunopotentiators**

Immunopotentiators are the substances that stimulate innate immune system. Traditionally, the term adjuvant has been used to describe any molecule that improves the immune response to co-administered antigen. Adjuvants can improve the effectiveness of vaccines by accelerating the generation of robust immune response, sustaining responses for longer duration, generating antibodies with increased avidity and neutralization capacity eliciting cytotoxic T lymphocytes and enhances the
immune response in humans as well as in animals. The adjuvants are broadly classified as follows

- Mineral salts, e.g. aluminium salts (aluminium hydroxide and aluminium phosphate gels) or calcium phosphate gel.
- Oil emulsions and surfactant based formulations e.g. micro fluidised detergent stabilised oil in water emulsion (MF 59), purified saponin (QS 21), AS02 (oil-in-water emulsion + MPL + QS 21).
- Particulate adjuvants e.g. virisomes (unilamellar liposomal vehicles incorporating influenza haemagglutinin, aluminium salts, Freund's incomplete adjuvant, Immune Stimulating Complexes (ISCOM).

Currently, alum is the only adjuvant approved for clinical use, even though calcium phosphate and oil emulsions also comprise some use in human immunization. Alum is not a universal adjuvant as it is not suitable for small peptides and alum adsorbed vaccines elicit short lasting immune response, which requires booster dose. Moreover, alum can induce the formation of granuloma at the site of injection and stimulate the production of IgE antibodies, which are mediating immediate hypersensitivity reactions. It is not suitable for small peptides and recombinant proteins. In addition alum cannot be frozen or lyophilized. Therefore, it is necessary to find out an alternative adjuvant for vaccine delivery, which must give a long lasting immune response after a single administration of vaccine.

**A view on biodegradable polymers**

The concept of drugs and vaccine delivery system has been developed tremendously during the past two decades. In controlled release technology, biodegradable polymers offer potential advantages for prolonged effect of drugs and vaccines. Polymers are applied for a large number of medical applications: as medical
supplier, as support or replacement of malfunctioning body parts or as a drug reservoir providing a local therapeutic effect. Currently, biodegradable polymers represent a class of ubiquitous materials and are being used for a multitude of purposes, because of increased interest being shown by the pharmaceutical industry for the fabrication of vaccine delivery system. A variety of natural and synthetic polymers have been investigated for sustained release of vaccines. Among these polymers, chitin and chitosan are natural polymers, whereas poly lactic acid (PLA), poly glycolic acid (PGA), poly (lactide – co – glycolide) (PLGA), poly caprolactone (PCL), etc are synthetic polymers.

1. **Poly (lactide – co – glycolide) (PLGA)**

   PLGA is a biocompatible and biodegradable synthetic polymer. Poly (d, l-lactide-co-glycolide) is a polymeric ester of the two hydroxyacids viz lactic and glycolic acids. PLGA degrades through bulk erosion to produce lactic and glycolic acid in aqueous solution leads to the release of the two acids, which can be metabolized via the citric acid cycle. It is approved by food and drug administration, United States for therapeutic devices. PLGA degrades by hydrolysis for its ester linkages in the presence of water, which gives lactic acid and glycolic acid. These two monomers under normal physiological conditions are byproducts of various metabolic pathways in the body. Therefore, the human body effectively deals with these monomers.

2. **Poly lactic acid (PLA)**

   PLA is biodegradable, biocompatible, thermoplastic, aliphatic polyester derived from lactic acid. It is frequently used in bone repair applications. The polymer chains are cleaved by hydrolysis to form monomeric acids and are eliminated from the body through Krebs’s cycle, as carbon di oxide through respiration and water in
urine. The rate of hydrolysis of the polymer chain is dependent on significant
temperature, pH or presence of catalyst.

3. Chitosan

Chitosan is a natural polymer, which possesses valuable properties and
obtained by alkaline deacetylation of chitin from shrimp or crab shells. It is poly β-
(1→ 4)-2-amino-2-deoxy-glucopyranose and has been reported for medical and
pharmaceutical applications. The typical commercial chitosan has approximately 85%
deacetylation and available in the form of dry flakes, solution and fine powder. It is
insoluble in water but soluble in acidic pH and therefore, acetic acid has been used as
solvent for chitosan. Due to the easy availability of free amino groups in chitosan, it
carries a positive charge and thus in turn reacts with many negatively charged
surfaces/polymers and also undergoes chelation with metal ions. Properties such as
biodegradability, low toxicity and good biocompatibility make it suitable for use in
biomedical and pharmaceutical formulations. Since chitosan has a capacity of forming
film it has been suggested as a biopolymer of choice for the development of contact
lens. Chitosan membranes have also been found useful as artificial kidney membranes
because of their suitable permeability and high tensile strength. Chitosan polymer of
different viscosities (50 cps, 150 cps and 300 cps) were used in this research work to
encapsulate hepatitis B vaccine.

4. Albumin

Albumins are widely distributed in plant and animal tissues, e.g., ovalbumin of
egg, myogen of muscle, serum albumin of blood, lactalbumin of milk, legumelin of
peas, and leucosin of wheat. Separation of serum albumins from other blood proteins
can be carried out by electrophoresis or by fractional precipitation with various salts.
Albumins normally constitute about 55% of the plasma proteins and adhere
chemically to various substances in the blood, e.g., amino acids, and thus play a role in their transport.

5. **Dextran**

Dextran is a complex, branched polysaccharide made of many glucose molecules joined into chains of varying lengths. The straight chain consists of $\alpha 1 \rightarrow 6$ glycosidic linkages between glucose molecules, while branches begin from $\alpha 1 \rightarrow 3$ linkages (and in some cases, $\alpha 1 \rightarrow 2$ and $\alpha 1 \rightarrow 4$ linkages as well). Dextran is synthesized from sucrose by *Leuconostoc mesenteroides* and *Streptococcus mutans* and are also produced by other bacteria and yeast.

**Microparticle system**

Biodegradable polymers are being used as sutures and drug carriers, because of the nontoxic nature and their adjustable biodegradable properties. The polymers chosen as excipients for parenterally administered particles should meet some requirements, including being biodegradable, safe (tissue compatible, no secondary reaction), drug compatible and permeable, stable *in vitro* easy to process, alone responsible formulations and ideally inexpensive. The biodegradable synthetic and natural polymers have been investigated for the control release of macromolecular drugs. These polymers in the form of microspheres seem to prefer for better controlled release of vaccine. New vaccines based on recombinant proteins and DNA, are safer than traditional vaccines, but they are less immunogenic. Therefore, there is an urgent need for the development of potent and safe adjuvants and delivery systems that can be used to boost up the immune response of vaccines. Polymer microspheres have shown great potential as a next generation adjuvant to replace or complement existing aluminium salts for vaccine potentiation. Microspheres are solid, spherical or approximately spherical particles ranging in size from 1 to 1000 $\mu$m.
based systems can now be made to deliver subunit protein and peptide antigens in their native form in a continuous or pulsatile fashion for periods of weeks to months. The vaccine release from microparticles regulates the therapeutic action. However, the release rate is greatly influenced by vaccine loading, polymers molecular weight, particle size and porosity. In fact, controlled release systems can provide a release of antigens for weeks to months, a time far exceeding the depot effect of aluminium salts or water/oil emulsions such as Freund’s adjuvants. In addition, the prolonged and pulsatile release of vaccine from microparticles may mimic the priming and boosting effect of conventional vaccines.

**Objectives of the present study**

The decision to introduce a vaccine into EPI is greatly influenced by a number of factors such as disease burden, epidemiological aspects with special reference to transmission, vaccine factors that includes safety, efficacy and availability, feasibility of introduction, financial implications, and projected or expected benefits in terms of morbidity, mortality and cost effectiveness. Thus a vaccine that is ideal for introduction into EPI would be one that is highly efficacious, economical, safe and protects against disease. Accordingly, a safe vaccine against hepatitis B virus infection has been made available for nearly 20 years. But it requires three doses, which must be given at 0, 1, and 6 months to elicit an optimum immune response. However, immune response gradually declines with increasing age. Besides, repeated immunizations may result in seroconversions. Moreover, alum is the only adjuvant approved for clinical use, but alum is not a universal adjuvant as it is not suitable for small peptides. It is therefore necessary to find out an alternative adjuvant, which gives long lasting immune response after a single administration of vaccine is therapeutically and economically very important. However, the price of
hepatitis B vaccine varies a lot in the open market, especially between domestic and multi national companies. The cost of hepatitis B vaccine is several folds (between 15 to 107 times) more than the cost of DTP vaccine in the open market. Therefore, the cost of vaccine, immunization programme deterrent to global immunization programme to combat hepatitis B.

Based on this, Global Alliance for Vaccines and Immunization (GAVI) has recommended the combined DTP – hepatitis B vaccine in order to reduce the cost of vaccines and cold chain. In principle, it is a good idea, to the extent that it shortens the immunization schedule and makes it more convenient to the health workers as well as the people. Unfortunately, the cost of combined DTP - hepatitis B vaccine is considerably more when compared to separate DTP and hepatitis B vaccine. Vaccine development and immunization constitute critical components of the public-health policy in any country and is more so in developing countries, where the government makes and/or buys most vaccines. Yet, recent decades have witnessed a growing gap between demand and supply of primary vaccines, attributable in part to the decline of the public sector and the disinterest of the bound on private sector in primary vaccines in favour of more lucrative new vaccines, such as that for hepatitis B. Viral Hepatitis Prevention Board (VHPB) in 2001 recommended a hexavalent vaccine comprising hepatitis B, haemophilus influenza type B, DTP and inactive polio virus in order to improve vaccination coverage, avoiding unnecessary injections, reducing cold chain, decreased waste and increased safety. On account of these advantages, the decision to use combined vaccine again becomes a debate, because conventional hepatitis B vaccine requires 3 doses to elicit maximum immune response. The immunization schedule may vary with perinatal transmission of hepatitis B. Countries like America, Europe, Africa and Central Asia, the three hepatitis B vaccine doses may commence
with DTP. In areas of high perinatal transmission such as China, East Asia etc the first
dose of hepatitis B vaccine must be given soon after birth. Moreover, DTP cannot be
However, the immune response gradually declines with increasing age. Therefore, the
magnitude of hepatitis B vaccine throughout the life is again a debate. Considering
these drawbacks the following objectives will be fulfilled in this study.
a) To develop a single contact hepatitis B vaccine as the most urgent need of
   Expanded Programme of Immunization (EPI) to control hepatitis B.
b) To find out a suitable method, suitable polymer and to standardize the
technique for formulating the single contact hepatitis B vaccine.
c) To develop single contact hepatitis B vaccine mainly administered during
   childhood and to effectively protect from hepatitis B
d) As postulated by World Health Organization for vaccine development – It is
   an attempt against hepatitis B.

Immunization programmes aim to reduce mortality and morbidity due to
vaccine preventable diseases. Delivering effective and safe vaccines through an
efficient delivery system is one of the most cost effective health arbitrations. The
biodegradable synthetic and natural polymeric microparticles are preferred for the
better controlled delivery of vaccines, which mimics both prime and boosting dose of
conventional vaccine. Based on these factors the development of single contact
hepatitis B vaccine based on biodegradable polymers is very important advancement
towards the betterment of human health care.