Vaccine compositions and processes are disclosed for culturing the pathogenic bacteria containing virulent capsular polysaccharides in animal free culture medium, isolation, purification of polysaccharides and polysaccharide-protein conjugate. The purification of capsular polysaccharides may or may not employ alcohol for preparing immunogenic formulations. The immunogens obtained from the process of the invention were formulated and do not contain any sources of animal-origin and alcohol excipients. Also disclosed is a method for isolation, purification and conjugation of bacterial capsular polysaccharide of Haemophilus influenza. The novel processes for purification, removal of endotoxin and formation of immuno-conjugates have also been used to generate novel compositions responsible to invoke immunogenicity against infections against Hib and prevention and treatment thereof.

The present invention also relates to the production and use of such vaccines for prophylaxis against the infections mentioned above.

Vaccine compositions with buffers of the invention are stable liquid rotavirus vaccine formulations for oral administration.

Invention provides rotavirus vaccine compositions comprising rotavirus antigens, stabilizers and buffers. The buffers in the invention are pre-mixed in the rotavirus vaccine compositions to neutralize the high acidic pH of the stomach without, requiring separate administration of an antacid before vaccine administration.

Vaccine compositions and processes are disclosed for culturing the pathogenic bacteria containing virulent capsular polysaccharides in animal free culture medium, isolation, purification of polysaccharides and polysaccharide-protein conjugate. The purification of capsular polysaccharides may or may not employ alcohol for preparing immunogenic formulations. The immunogens obtained from the process of the invention were formulated and do not contain any sources of animal-origin and alcohol excipients. Also disclosed is a method for isolation, purification and conjugation of bacterial capsular polysaccharide of Haemophilus influenza. The novel processes for purification, removal of endotoxin and formation of immuno-conjugates have also been used to generate novel compositions responsible to invoke immunogenicity against infections against Hib and prevention and treatment thereof.

Vaccine compositions and processes are disclosed for culturing the pathogenic bacteria containing virulent capsular polysaccharides in animal free culture medium, isolation, purification of polysaccharides and polysaccharide-protein conjugate. The purification of capsular polysaccharides may or may not employ alcohol for preparing immunogenic formulations. The immunogens obtained from the process of the invention were formulated and do not contain any sources of animal-origin and alcohol excipients. Also disclosed is a method for isolation, purification and conjugation of bacterial capsular polysaccharide of Haemophilus influenza. The novel processes for purification, removal of endotoxin and formation of immuno-conjugates have also been used to generate novel compositions responsible to invoke immunogenicity against infections against Hib and prevention and treatment thereof.
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<th>Inventor</th>
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<td>7.</td>
<td>A NOVEL SYNERGISTIC PHARMACEUTICAL COMPOSITION FOR TOPICAL APPLICATIONS</td>
<td>10.04.2013</td>
<td>BHARAT BIOTECH INT LTD</td>
<td>MOHAN VAIDREPU, KRISHNA</td>
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<td>NOVEL SYNERGISTIC PHARMACEUTICAL COMPOSITION FOR TOPICAL APPLICATIONS</td>
<td>04.04.2013</td>
<td>Mohamed Vaidrepu, Krishna</td>
<td>Mohamed Vaidrepu, Krishna</td>
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<td>10.</td>
<td>VACCINE COMPOSITION COMPRISING AN INACTIVATED CHIKUNGUYA VIRUS STRAIN</td>
<td>20.12.2012</td>
<td>BHARAT BIOTECH INTERNATIONAL LIMITED</td>
<td>ELLA, Krishna Murthy</td>
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<td>11.</td>
<td>COMPOSICIÓN DEL FATOR DE CRESCIMENTO EPIDÉMICO, O PROCESSO PARA ISSO E SUA APLICAÇÃO</td>
<td>30.10.2012</td>
<td>BHARAT BIOTECH International Limited</td>
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<td>12.</td>
<td>COMPOSICÃO DO FATOR DE CRESCIMENTO EPIDÉMICO, O PROCESSO PARA ISSO E SUA APLICAÇÃO</td>
<td>14.08.2012</td>
<td>BHARAT BIOTECH International Limited</td>
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<td>14.</td>
<td>VACCINE FORMULATION FOR PROPHYLAXIS AND TREATMENT OF CHANDIPURA VIRUS INFECTIONS IN MAMMALS</td>
<td>07.06.2012</td>
<td>BHARAT BIOTECH INTERNATIONAL LIMITED</td>
<td>ELLA, Krishna Murthy</td>
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The present invention is related to pharmaceutical formulations capable of eliciting protective immune response against Chandipura virus infection in humans and other mammalian hosts. The immunogenic formulation comprises Chandipura virus glycoprotein (G protein) and/or nucleoprotein (N protein) expressed as recombinant proteins and purified from host cells. Vaccine compositions comprising the recombinant proteins elicit neutralizing antibodies similar to the vaccine compositions of purified inactivated Chandipura virus in a stable formulation. Methods of inactivating Chandipura virus for use as a candidate vaccine are disclosed. The vaccine compositions have been formulated with adjuvants to potentiate the immune response. The vaccine compositions disclosed in the invention are highly immunogenic and elicit protective immune response in mammalian host. The immunogenic compositions are formulated for use in veterinary administration to humans. The immunogenic preparation will also find use in diagnosing for the presence of the virus.

A novel synergistic pharmaceutical composition for preparation of topical formulations for prophylaxis and treatment of wounds, burn wounds, skin grafts, pressure ulcers and diabetic foot ulcers is disclosed. The synergistic composition comprises a mitogenic protein in combination with one or more bactericidal and bacteriostatic agents. The mitogenic protein in the invention is Recombinant Human Epidermal Growth Factor (rh-EGF) of Bharat Biotech International Limited and/or any other growth factor like rh-PDGF-BB and the bactericidal and bacteriostatic agents are broad spectrum antibiotics silver sulfadiazine (SSD) and chlorhexidine gluconate (CHG). The topical formulations, in addition to the synergistic composition, also comprise base ingredients, carriers, preservatives, emulsifiers, skin emollients and soothers and one or more other constituents. The novel composition results in synergistic effects like broader antibacterial coverage, reversal of silver effect of SSD by rh-EGF, effectiveness against silver resistant microorganisms in burn wounds, and better and faster wound healing. The novel composition may be used to prepare the topical formulations in the form of cream, gel or liquid. The novel formulations have longer shelf life and are stable for more than two years at the storage temperature of 2-8° degrees.

A novel synergistic pharmaceutical composition for preparation of topical formulations for prophylaxis and treatment of wounds, burn wounds, skin grafts, pressure ulcers and diabetic foot ulcers is disclosed. The synergistic composition comprises a mitogenic protein in combination with one or more bactericidal and bacteriostatic agents. The mitogenic protein in the invention is Recombinant Human Epidermal Growth Factor (rh-EGF) of Bharat Biotech International Limited and/or any other growth factor like rh-PDGF-BB and the bactericidal and bacteriostatic agents are broad spectrum antibiotics silver sulfadiazine (SSD) and chlorhexidine gluconate (CHG). The topical formulations, in addition to the synergistic composition, also comprise base ingredients, carriers, preservatives, emulsifiers, skin emollients and soothers and one or more other constituents. The novel composition results in synergistic effects like broader antibacterial coverage, reversal of silver effect of SSD by rh-EGF, effectiveness against silver resistant microorganisms in burn wounds, and better and faster wound healing. The novel composition may be used to prepare the topical formulations in the form of cream, gel or liquid. The novel formulations have longer shelf life and are stable for more than two years at the storage temperature of 2-8° degrees.

Compositions and methods related to live or live attenuated pre-conditioned and typical viruses such as rotaviruses are disclosed. The live attenuated rotaviruses compositions have been formulated with adjuvants to potentiate the immune response. The vaccine compositions disclosed in the invention are highly immunogenic and elicit protective immune response in mammalian host. The immunogenic compositions are formulated for use in veterinary administration to humans. The immunogenic preparation will also find use in diagnosing for the presence of the virus.

Compositions and methods related to live or live attenuated pre-conditioned and typical viruses such as rotaviruses are disclosed. The live attenuated rotaviruses compositions have been formulated with adjuvants to potentiate the immune response. The vaccine compositions disclosed in the invention are highly immunogenic and elicit protective immune response in mammalian host. The immunogenic compositions are formulated for use in veterinary administration to humans. The immunogenic preparation will also find use in diagnosing for the presence of the virus.

The invention describes a stable immunogenic protein having multiple cysteine molecules wherein the protein is having stability up to two years and purity more than 98% particularly rPvRII and/or rPfF2. It also discloses a method for producing said immunogenic protein comprising the following steps: culturing the host E.coli cells containing a desired recombinant gene construct comprising a codon optimized gene sequence of rPvRII and/or rPfF2 to produce cells in high density; inducing expression of rPvRII and/or rPfF2 as inclusion bodies; harvesting the cells and isolating the said inclusion bodies; separating rPvRII and/or rPfF2 from inclusion bodies by repeated sequential washing and solubilizing with chaotropic agents comprising guanidine hydrochloride and/or 1M urea; purifying the protein by subjecting to metal-chelate affinity chromatography; re-folding of the purified rPvRII and/or rPfF2 obtained in step e) with a redox system to recover a high yield of the soluble protein, followed by further purifying the desired protein by removing impurities by subjecting to chromatography. Further the invention discloses formulation comprising rPvRII and/or rPfF2, preferably being lyophilized using polysaccharides preferably sucrose, lactose, and pharmaceutically acceptable adjuvants such as aluminum hydroxide, aluminum phosphate, CpG nucleotides, non-CpG nucleotides, Montanide ISA-720, MF-59, Mono-phosphoryl Lipid-A (MPL-A) and QS-21.

Compositions and methods related to live or live attenuated pre-conditioned and typical viruses such as rotaviruses are disclosed. The live attenuated rotaviruses compositions have been formulated with adjuvants to potentiate the immune response. The vaccine compositions disclosed in the invention are highly immunogenic and elicit protective immune response in mammalian host. The immunogenic compositions are formulated for use in veterinary administration to humans. The immunogenic preparation will also find use in diagnosing for the presence of the virus.

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Compositions and methods related to live or live attenuated pre-conditioned and typical viruses such as rotaviruses are disclosed. The live attenuated rotaviruses compositions have been formulated with adjuvants to potentiate the immune response. The vaccine compositions disclosed in the invention are highly immunogenic and elicit protective immune response in mammalian host. The immunogenic compositions are formulated for use in veterinary administration to humans. The immunogenic preparation will also find use in diagnosing for the presence of the virus.
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<th>Applicant</th>
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<td>22</td>
<td>US</td>
<td>NOVEL THROMBOLYTIC MOLECULES AND A PROCESS THEREFOR</td>
<td>21.01.2010</td>
<td>A61K 38/43</td>
<td>12300150</td>
<td>BHARAT BIOTECH INTERNATIONAL LIMITED</td>
<td>Ella Krishna Murthy</td>
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New thrombolytic protein molecules such as recombinant staphylokinase or streptokinase, urokinase, tissue plasminogen activator and the like, and suitable variants thereof, for targeting to brain tissue or any other tissue by either fusing to, or by synthesizing the candidate thrombolytic molecule(s) with a protein sequence comprising a strong amphipathic alpha helix containing protein transduction domain. Thrombolytic protein molecule(s) so engineered with the protein transduction domain is useful for enhanced uptake of such protein thrombolytic molecule(s) across the cell membranes and tissues including the blood brain barrier and find their use in the treatment of vascular thrombosis including cerebrovascular disorders caused by cerebral thrombosis or cerebral hemorrhage when used as a therapeutic. The design and processes for cloning, expression, purification and protein transduction of such proteins across cell membranes.


The invention describes a vaccine compositions comprising chimeric fusions of the HPV antigens with viral or bacterial proteins conferring enhanced immunogenicity useful for Hepatitis B virus as well as human papillomavirus (HPV) infections.

24. US 2008020538 - VACCINE FOR STAPHYLOCOCCAL INFECTIONS | 03.09.2009 | A61K 39/085 | 12067458 | BHARAT BIOTECH INTERNATIONAL LIMITED | Ella Krishna Murthy |

The present invention describes method of preparation and use of polypeptide vaccine formulation for prevention and control of Staphylococci mediated infections in human, bovine and other mammals, using recombinant DNA technology.

25. MX MX/a/2008/014391 - A COMPOSITION USEFUL AS A VACCINE | 13.05.2009 | A61K 39/15 | MX/a/2008/014391 | BHARAT BIOTECH INTERNATIONAL LIMITED | ELLA, Krishna, Murthy |

The present invention relates to a composition comprising a viral antigen, a first protein and a second protein. Optionally, the composition also comprises three different disaccharides, or, optionally, the composition comprises a primary sugar and at least one, preferably two secondary sugars. The present invention also relates to the use of a viral antigen, a first protein and a second protein for the manufacture of a composition, preferably a vaccine. The present invention furthermore relates to a method of treatment or prevention of virus associates diseases in humans. Moreover, the present invention relates to a method of adapting a virus to a suitable cell-line. The invention is also useful for the production of virus suspensions suitable for making stable, live/inactivated, monovalent and/or polyvalent, liquid/lyophilized rotavirus vaccine compositions for oral and/or nasal or any other suitable route of administration in human.


A composition for treating a wound, wherein the composition can comprise therapeutically effective amount of an epidermal growth factor and a physiologically acceptable agent, wherein the physiologically acceptable agent comprises at least one of a stabilizer, a preservative, a thickening agent, carrier/diluent, and optionally pH regulating agent and humectant.

27. WO WO/2008/026225 - A VACCINE FOR CHIKUNGUNYA VIRUS INFECTION | 06.03.2008 | A61K 39/12 | PCT/IN2007/000383 | BHARAT BIOTECH INTERNATIONAL LIMITED | ELLA, Krishna, Murthy |

The present invention relates to vaccine formulation capable of eliciting protective immune response against Chikungunya virus infection in humans and other mammalian hosts. The immunogenic formulation comprises purified inactivated Chikungunya virus in a stable formulation. Methods of propagation and purification of the virus is discussed. The inactivated virus formulation is non-infectious, immunogenic and efficic protective immune response in mammalian host. The immunogenic composition is formulated for in vivo administration to humans. The invention also discusses the strategy of developing a subunit vaccine using the recombinant viral proteins as antigens for immunization. The recombinant virus antigens that are potentially immunogenic can be used in diagnosing for the presence of the virus.

28. US 20070275006 - IRIDOID GLYCOSIDE COMPOSITION | 29.11.2007 | A61K 45/00 | 11683975 | COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH | Khajuria Anamika |

The present invention relates to an adjuvants, particularly to the use of a well-characterized plant based iridoid glycoside adjuvant from plant Picrorhiza kurroa, acting as an adjuvant against T-dependent antigen and specifically against HBsAg and typhoid antigens. The present invention also relates to the method of producing the iridoid glycoside adjuvant and the products utilizing such adjuvants for induction of cellular immunity. The adjuvants may be used alone or with specific antigens. The two antigens used in the study represents HBsAg, a recombinant antigen expressed in Pichia pastoris, and typhoid Vi polysaccharide purified from Salmonella typhi broth. These antigens are studied for their immunogenicity with the adjuvant iridoid glycoside adjuvant.
The present invention relates to a composition comprising a viral antigen, a first protein and a second protein. Optionally, the composition also comprises three different disaccharides, or, optionally, the composition comprises a primary sugar and at least one, preferably two secondary sugars. The present invention also relates to the use of a viral antigen, a first protein and a second protein for the manufacture of a composition, preferably a vaccine. The present invention furthermore relates to a method of treatment or prevention of virus associates diseases in humans. Moreover, the present invention relates to a method of adapting a virus to a suitable cell-line. The invention is also useful for the production of virus suspensions suitable for making stable, live/inactivated, monovalent and/or polyvalent, liquid/solidified rotavirus vaccine compositions for oral and/or nasal or any other suitable route of administration in human.

30. WO PCT/IN2004/000257 - NOVEL THROMBOLYTIC MOLECULES AND A PROCESS THEREOF 22.11.2007 C07K 14/31 BHARAT BIOTECH INTERNATIONAL LIMITED ELLA, Krishna, Murthy

The invention discloses a new THROMBOLYTIC protein molecules such as recombinant staphylokinase or streptokinase, urokinase, tissue plasminogen activator and the like, and is suitable to their variants thereof, for targeting to brain tissue or any other tissue by either fusing to, or by synthesizing the candidate thrombolytic molecule(s) with a protein sequence comprising a strong amphipathic alpha helix containing protein transduction domain. Thrombolytic protein molecule(s) so engineered with the protein transduction domain is useful for enhanced uptake of such protein thrombolytic molecule(s) across the cell membranes and tissues including the blood brain barrier and find their use in the treatment of vascular thrombosis including cerebrovascular disorders caused by cerebral thrombosis or cerebral haemorrhage when used as a therapeutic. The invention discloses the design and processes for cloning, expression, purification and protein transduction of such proteins across cell membranes.

31. WO PCT/IN2006/000246 - A VACCINE FOR STAPHYLOCOCCAL INFECTIONS 18.01.2007 C07K 14/31 BHARAT BIOTECH INTERNATIONAL LIMITED ELLA, Krishna, Murthy

The present invention describes method of preparation and use of polyopeptide vaccine formulation for prevention and control of Staphylococci mediated infections in human, bovine and other mammals, using recombinant DNA technology. © KIPO & WIPO 2007


A novel process for the purification of recombinant protein expressed as protein or particle is herewith described. In this purification process, the protein is purified by hydrophobic interaction. The interaction of this protein step resulted in an increase in recovery and purity from 15%-80%. The protein further purified has its application in vaccines and pharmaceuticals.


A composition for treating a wound, wherein the composition can comprise therapeutically effective amount of an epidermal growth factor and a physiologically acceptable agent, wherein the physiologically acceptable agent comprises at least one of a stabilizer, a preservative, a thickening agent, carrier/diluent, and optionally pH regulating agent and humectant.

34. WO PCT/IN2004/000255 - EUKARYOTIC BASED SYNERGISTIC FORMULATION FOR GASTRO-INTESTINAL DISORDERS 02.03.2006 A61K 36/062 BHARAT BIOTECH INTERNATIONAL LIMITED ELLA, Krishna, Murthy

The present invention describes a eukaryotic based synergistic formulation for gastro-intestinal disorders comprising eukaryotics and adjuncts selected from pharmaceutically and/or physiologically acceptable components. The invention also describes the manner in which the eukaryotics are isolated from tropical fruits, The medium used for growing them and the method used to convert the formulation to dispensable forms. The medium comprising Glucose for carbon source, soybean casein dextrose medium (SCDM) for Nitrogen source, MgSO4, KCl, NaCl, (NH)4HPO4 and with microelements like MnSO4, FeSO4, CuSO4, Boric acid and Vitamins, D-Biotin and thiamine HCl ranging from 0.001% to 0.6% and designated as BBIL-SB. The formulation can be effectively used to prevent and/or cure gastro intestinal disorders by administering in various forms to the mammals including human suffering there from, in a required quantity.


An Indian isolate of Hepatitis A virus - NIVIN97 has been isolated, adapted to tissue culture, characterized and further propagated using Vero and MRC-5 cell lines for vaccine preparation. The method involves the cell culture adaptation of the virus isolate from clinical sample (faeces) in BGMK cell line initially, characterization of the virus and further adaptation to Vero and MRC-5 cells, scale-up, activation and down stream processing method of the inactivated viral antigens for the preparation of an inactivated vaccine.


A novel process for the purification of recombinant protein expressed as protein or particle is herewith described. In this purification process, the protein is purified by hydrophobic interaction. The interaction of this protein step resulted in an increase in recovery and purity from 15%-80%. The protein further purified has its application in vaccines and pharmaceuticals.

37. CA 2548378 - A PROCESS FOR THE PREPARATION AND PURIFICATION OF RECOMBINTAN PROTEINS 14.07.2005 C07K 1/30 BHARAT BIOTECH INTERNATIONAL LIMITED ELLA, KRISHNA MURTHY

The present invention describes method of preparation and use of polypeptide vaccine formulation for prevention and control of Staphylococci mediated infections in human, bovine and other mammals, using recombinant DNA technology. © KIPO & WIPO 2007
A novel process for the purification of recombinant protein expressed as protein or particle is herewith described. In this purification process, the protein is purified by hydrophobic interaction. The interaction of this protein step resulted in an increase in recovery and purity from 15%-80%. The protein further purified has its application in vaccines and pharmaceuticals.

A portion of the lysostaphin gene of *Staphylococcus simulans* has been cloned and overexpressed in the cytoplasm of *E. coli* to yield lysostaphin, in the absence of preprolysostaphin and prolysostaphin, under the transcriptional control of an IPTG-inducible promoter and a ribosome binding site. IPTG induction of the transformed host cells produces intracellular, soluble, mature lysostaphin (27 kDa), in the complete absence of preprolysostaphin and prolysostaphin. The mature lysostaphin so formed does not require post-translational modification. The mature lysostaphin so formed can be used to treat and prevent staphylococcal infections.